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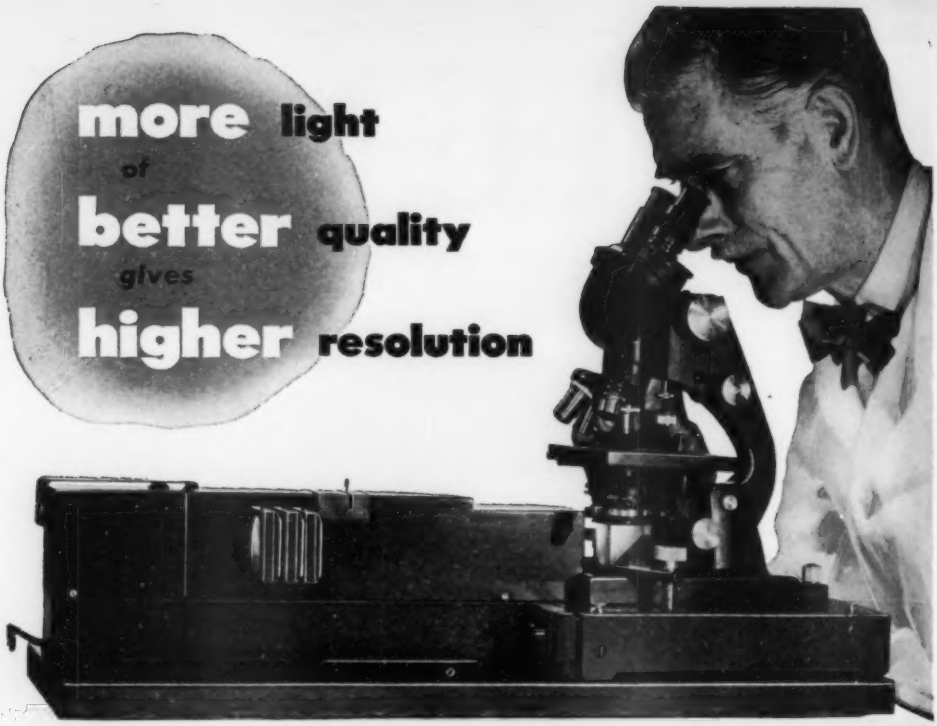

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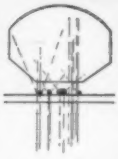

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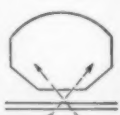

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Being an institute specifically concerned with agriculture, our membership naturally covers a narrower field of interest than the AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, but a surprising number of disciplines are represented in our membership because of the demands that scientific agriculture makes on the field of science generally. The institute endeavors to do its part in the fostering of scientific agriculture by encouraging a national policy of agricultural research, promoting interchange of ideas between scientists both within the Commonwealth and overseas, representing the views of the profession, maintaining its integrity, and raising its status. In our efforts to achieve these aims we have engaged in a number of activities, including professional evidence on agricultural education, a survey of the agricultural resources of the Commonwealth, a review of plant quarantine, with recommendations and reviews of the roles of the agricultural engineer and agricultural extension services in Australian agriculture. The reports resulting from these projects have helped directly to guide governments in agricultural legislation and administration and have assisted members of the institute to crystallize their own ideas on topics with which they are concerned.

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JOHN M. STEVENS
The Journal of the Australian Institute of Agricultural Science
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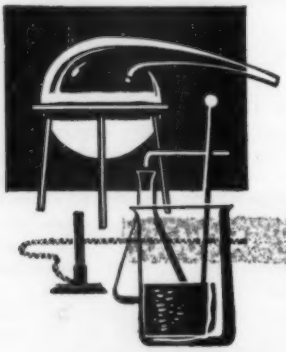

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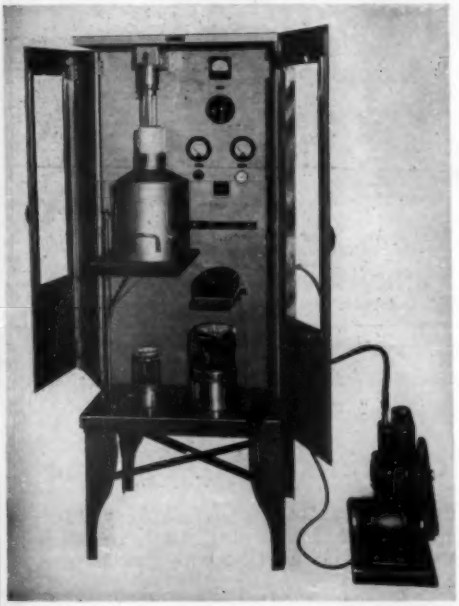

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Irradiation of Parts of Individual Cells[1]

Raymond E. Zirkle and William Bloom[2]

Institute of Radiobiology and Biophysics and *Department of Anatomy, University of Chicago, Chicago, Illinois*

SELECTIVE EXPOSURE of fractions of intact individual cells to high-energy radiation is of interest for two reasons. First, it has obvious use in radiobiology as a means of gaining information about the mechanisms by which radiations produce their strikingly injurious effects on living systems. Second, and of much more general application, it can aid in analyzing the normal functions of the various cell parts by selectively altering them. In this respect it complements microsurgery.

Irradiation of parts of single intact cells has been done before, both with ultraviolet light (*1*) and with high-energy radiation (*2–7*),[3] but in each instance the success of the technique has been largely dependent on some peculiarity of cell structure, e.g., exceptionally large size (*2, 7*) or an eccentric nucleus (*2, 3*), and accordingly has been quite limited in application. Also the cell fraction irradiated has in most cases been quite large (25–50 per cent). This paper contains a brief description of a new and widely applicable method with which considerably smaller fractions of average-sized cells can be bombarded, and mention of some of the results obtained.

Procedure

The method is based upon a *microbeam* of ionizing particles arranged to traverse a selected small portion of the individual cell under study. Obviously, the cross section of such a microbeam must be small compared to the cell area perpendicular to the beam's axis, i.e., it must have dimensions of the order of microns.

In general, to produce a microbeam of high-energy radiation, one must start with a beam of macroscopic dimensions and either focus all or part of it to a microscopic cross section or allow part to pass through a microaperture in a layer of impervious material. Neutrons do not lend themselves satisfactorily to either procedure. Nor do photons (x or γ rays), except for low-energy x rays from tubes of special design (*10*). This restricts the choice of radiation type to fast charged particles (electrons, mesons, or atomic nuclei such as protons, deuterons, or alpha particles). The mesons can be disregarded because no currently available source produces a sufficiently intense macrobeam. Electrons and atomic nuclei can be focused electrically and/or magnetically. However, this procedure was not tried because it appeared that the microbeam probably would have to be not only produced but used *in vacuo*; although some types of cells withstand vacuum very well, most do not, and formidable difficulties could be foreseen in trying to protect them from vacuum without creating difficulties in design of culture chambers. Accordingly, there remained the alternative of canalizing electrons or atomic nuclei with a microaperture. The electrons were ruled out because the macroscopic beam, impinging on the layer of material containing the microaperture, would produce x rays which would superimpose a very troublesome irradiation of the entire cell upon the localized irradiation with the microbeam. Moreover, electrons are very difficult to keep canalized satisfactorily, because of their great propensity for scattering when they collide with material of any sort. Accordingly, the fast atomic nuclei remained for consideration. Deuterons were not favorably regarded because of a probable health hazard due to the neutrons and other radiations that they would generate within the accelerator. The choice between protons and alpha particles (the currently available types of nucleus which remained) was largely dictated by the accelerator available, which was a vertical Van de Graaff electrostatic generator capable of producing 2-Mev protons or 4-Mev alpha particles, whose ranges in tissue are approximately 73 and 25 μ, respectively (*11*). Since, in most experiments, the particles had to traverse two mica windows equivalent in stopping power to 25 or 30 microns of tissue, it was clear that alphas would not be feasible. The protons remained as our best practical choice.

The macroscopic beam of protons emerged from the accelerator through a mica window 2 mm in diameter and 1.5 mg/cm^2 (5 μ) thick and was allowed to impinge on a metallic shield pierced by the microaperture. Several types of microaperture were investigated, of which two (G and XS) were considered satisfactory. Type G (Fig. 1) consisted essentially of two optically flat slit jaws *A*, across one of which a microscopic groove *B* either was scratched with a diamond or was "chopped" by means of a very carefully controlled collision with an optically polished blade. The two jaws were then firmly pressed together, leaving a microaperture of approximately triangular cross section. The position of the microaperture was marked by the intersection of the index

[1] This work was supported by grants from the U. S. Atomic Energy Commission, the Office of Naval Research, and the Abbott Research Fund, University of Chicago.

[2] The authors are deeply indebted to many persons, notably T. J. O'Donnell, J. V. Baaril, Joseph Getzholtz, John Costa, G. E. Moulson, C. E. Soderquist, Stefan Pichler, James Leider, Theresa Banny, Lily Wang, and Marion Park.

[3] We are here not directly concerned with certain interesting experiments (*8, 9*) in which cell parts have been separated mechanically before irradiation.

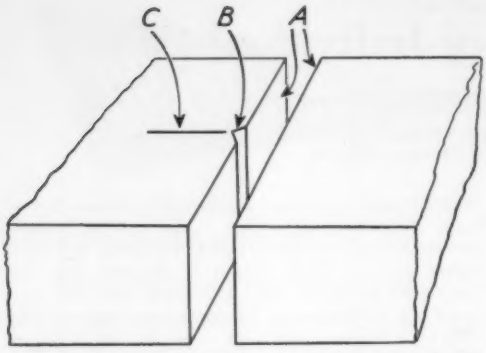

FIG. 1. Scheme of construction of a microaperture of type G. (See text.)

line C (lightly scratched on the metal) with the line of junction of the two jaws. Microapertures of type XS (Fig. 2) were formed of crossed slits, the jaws of which were polished to optical flatness. Each slit could be adjusted to any desired width from 0.5 μ to 5 mm by turning a graduated knob K.

The spatial distribution of the protons traversing each microaperture was determined by analysis of the pattern of tracks produced in Ilford C2 nuclear plates exposed at the position occupied by a cell during bombardment. Bombardment patterns for two type G microapertures are plotted in Fig. 3. The actual sizes of the microscopic holes were unknown and immaterial, but it will be noticed that, with each microaperture, when the bombarded object was 5–10 μ away from it, more than 80 per cent of the protons

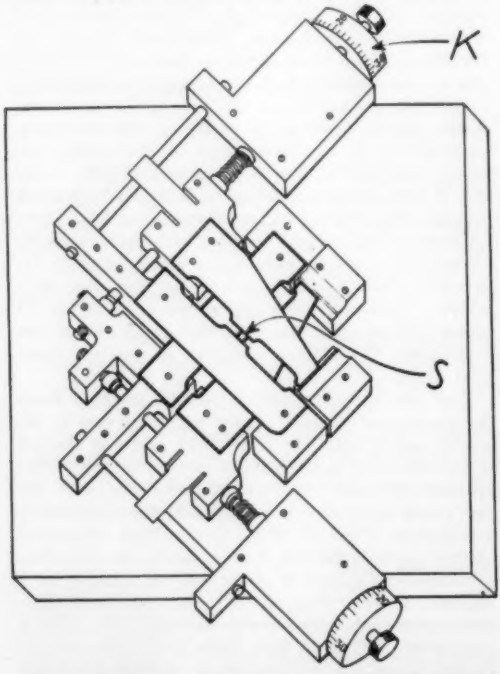

FIG. 2. Apparatus for producing variable microaperture of type XS (crossed slits). Both slits are shown open, their intersection at S. (See text.)

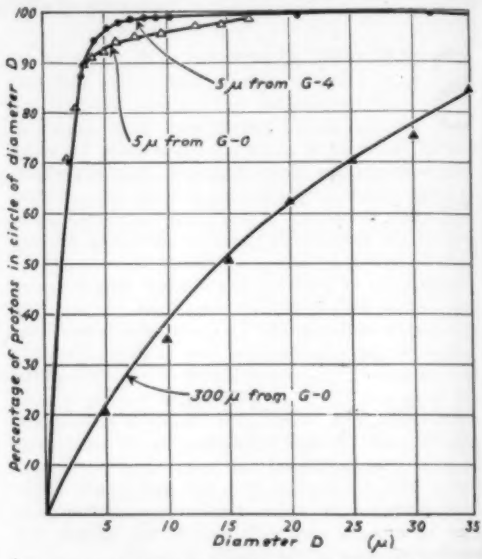

FIG. 3. Proton track distribution in nuclear plates exposed under two microapertures of type G. Note that, although the two yielded identical bombardment patterns at low angles of scatter, G-4 produced superior localization at high angles (two upper curves). Also note adverse effect of distance on localization produced by G-0.

struck a central area 2.5 μ in diameter. The tails of the curves represent protons scattered by atomic nuclei in the walls of the holes. This scattering cannot be eliminated but can be considerably reduced by improvements in geometrical design and in choice of material for the jaws. (Note that G-4 is much superior to G-0 in this respect.) The effect of scattering on the bombardment pattern has been minimized by placing the bombardment object as close as possible to the microaperture (note the great spread of the bombardment pattern when the plates were exposed 300 μ away). With microapertures of type XS, the bombardment patterns are well localized by the bottom slit but poorly by the upper (as in upper and lower curves, respectively, for G-0, Fig. 3). Type XS is excellent for bombardments in which a narrow "ribbon" microbeam is desired. Type G is superior when the microbeam must be essentially isodiametric in cross section.

For each microaperture the energy spectrum of the protons incident on the cell was determined by measuring the lengths of the individual tracks produced in Ilford C2 plates after the protons had passed through mica of the same thickness as that used for the cover

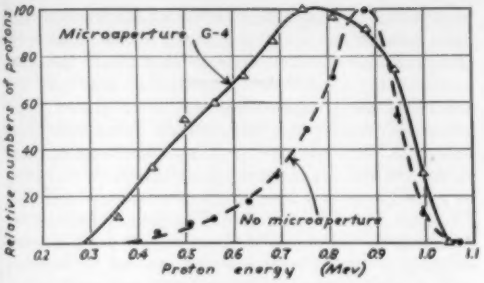

FIG. 4. Energy spectra of protons which traversed microaperture G-4 and of those which traversed no microaperture.

slips of the culture chambers. The spectrum of protons transmitted by microaperture G-4 is shown in Fig. 4, along with that of protons that passed through no microaperture.

In the microbeam bombardments the chief items of equipment were an *observation microscope* (Fig. 5) with which the cell was observed before and after bombardment; the *Van de Graaff generator* (*S*, Fig. 6); a *bombardment assembly* (Fig. 6) consisting of an *alignment microscope B*, a *bombardment stage C*, and a *microaperture assembly D*, all maintained in alignment by means of a rugged and precisely machined column *E*; a *master locator* (Fig. 7); and an *adjustable locator* (*AL*, Fig. 5) which bore the cell preparation on a small mechanical stage.

For reasons given below, it was essential that the cell for bombardment be directly beneath the cover slip of the cell preparation (tissue culture). When the culture was in bombardment position under the microaperture, the cell could be observed only from below, with vertical illumination. The thickness of the culture, dictated by various biological requirements, was so great that only a low-power objective could be focused on the cell. Moreover, the cell had to be observed through the entire thickness of culture medium and irrelevant cells, the result being poor optics. Accordingly, the notion of aiming the microbeam by direct observation of the cell in bombardment position was abandoned in favor of an indirect method of great flexibility and accuracy. In this procedure the master locator (Fig. 7) played a central role. This device consisted of a brass plate with a hole over which was securely fastened a glass slide whose upper surface was covered with a thin deposit of chromium. A microscopic cross *Q* was scratched through this metallic layer, near the middle of the slide. The brass plate was notched in such fashion that it could be brought into contact with three rounded and polished steel *stops T* (two shown in Fig. 6, all in Fig. 5) held in two *stop assemblies V* on the bombardment stage (Fig. 6) and also on the stage of the observation microscope (Fig. 5). A spring, attached to a corner of the stage and provided with a hook *H* (Figs. 5 and 6), was used to pull the plate, with a reproducible force, against the stops and to hold it securely in place. To provide a smooth surface and

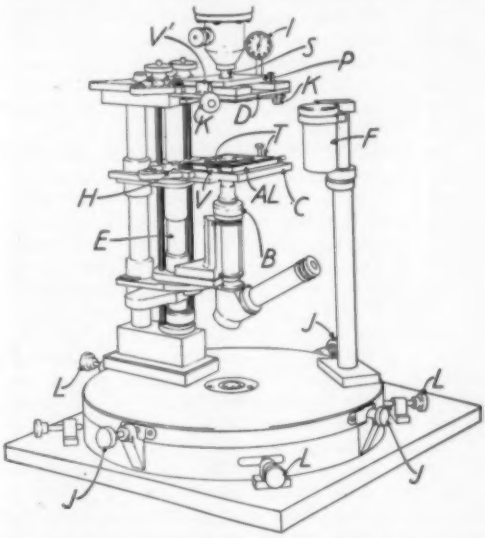

FIG. 6. Bombardment assembly. (See text.) *S*, delivery tube of Van de Graaff generator.

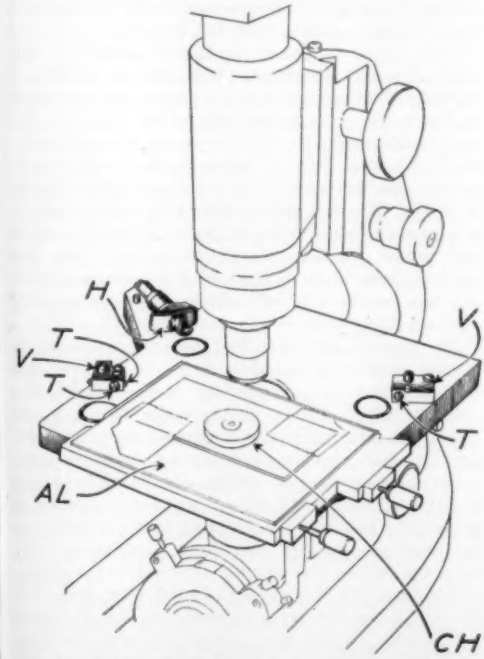

FIG. 5. Observation microscope, equipped for phase contrast. The stage is equipped with locator stops *T* and hook *H*. Adjustable locator *AL* detached from hook to show stops. Culture chamber *CH* mounted on locator.

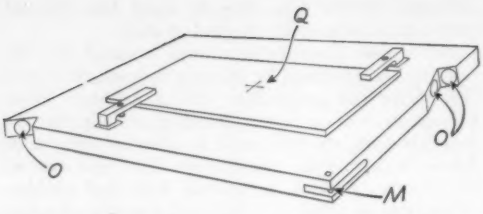

FIG. 7. Master locator. *M*, catch for hook *H* of Fig. 6. *O*, polished and hardened steel inserts. *Q*, position of microscopic cross. (Also see text.)

to prevent wear, the brass plate was provided with polished steel inserts *O* in the notches.

The master locator was hooked in place on the bombardment stage (*C*, Fig. 6), and the latter was raised to bombardment position. The alignment microscope *B* (800 × magnification) was raised and focused, through the hole in the brass locator plate, on the microscopic cross on the locator. If the image of the cross did not intersect the cross hairs in the ocular of the microscope, the stops were adjusted until it did.

The master locator was removed, and the alignment microscope was focused on the microaperture. If the cross hairs of the microscope did not intersect in the middle of the microaperture's image, the microaperture assembly, which was attached to a locator plate (*P*, Fig. 6) similar to the brass plate of the master locator, was suitably moved by adjustment of the stops *V'*. Since the cross on the master locator had also been lined up with the same cross hairs, the microbeam would have bombarded this microscopic cross if the master locator had been placed and hooked on the bombardment stage and the latter raised to bombardment position.

The master locator was now placed on the stage of the observation microscope (Fig. 5), which was provided with stops *T* and hooked spring *H* similar to those on the bombardment stage. If the image of the microscopic cross did not intersect the cross hairs of this microscope, the stops were suitably adjusted.

Now, if the master locator were removed and any other locator with identical notches were substituted, any small object on this latter locator would, if its image fell at the intersection of the cross hairs, be lined up with the microaperture when the locator was transferred to the bombardment stage. To eliminate any error due to slight deviations of the optical axes of the various observation microscopes, it was necessary that the microscopic cross *Q* on the master locator be the same height above the microscope stage as the object to be bombarded.[4]

Aiming was thus accomplished by an indirect method whose accuracy was determined by the precision with which the following operations could be performed: (1) alignment of the master locator with the microaperture; (2) alignment of the master locator and also of the bombarded object with the cross hairs of the observation microscope; and (3) the seating of the locators when they were shifted from one set of stops to another. All the lining-up operations could be made good to 0.2 μ. The reproducibility of the locators usually was equally good; if, as rarely happened, repeated tests of a locator's seating against the stops revealed reproducibility poorer than 0.2 μ, this was an indication that a contact point needed cleaning or that a stop assembly needed tightening; such servicing was readily accomplished and tested. The overall accuracy of aiming was accordingly no worse than 0.6 μ if all errors accumulated; since each error was random in direction, the various errors frequently compensated, and accordingly in most bombardments the aiming was better than 0.6 μ.

The microaperture was set in position in the main beam by means of adjusting screws (*L*, Fig. 6), which translated the entire bombardment assembly in two perpendicular horizontal directions, and was lined up with the beam by screws (*J*, Fig. 6), by which the axis of the bombardment assembly could be swung in two perpendicular vertical planes, the microaperture being located at the center of swing. These operations were facilitated by observing changes in proton flux through the microaperture by means of a Geiger-Müller counter with a mica window 5 μ (1.5 mg/cm²) thick (*F*, Fig. 6).

The cells were grown in tissue cultures of amphibian heart[5] (Triturus, Ambystoma). A culture chamber *CH* for microbeam bombardment is shown in Fig. 5. Since the penetration of the protons, after they had traversed the mica window of the generator, was only about 30 μ in water, the cover slip of the culture chamber was of mica 5 μ or slightly less in thickness. This left the protons with enough energy to traverse a cell, but it was essential that the cell be just below the mica cover. To ensure this, fine scratches were made on the top of the mica and selection was restricted to cells which were in focus along with a scratch in the same microscope field.

The experiments described here were limited to mitotic cells. With the observation microscope, each cell was carefully examined by medium-dark phase contrast, which clearly reveals many details in the amphibian cells, particularly chromosomes, mitochondria, nucleoli, nuclear membranes, chromatin particles, and sometimes the outline of the mitotic spindle and the cell centers. If the cell was found suitable in nature and location (not too deep in the culture, not too close to optically interfering neighboring cells, etc.), the culture was securely fastened to the adjustable locator (*AL*, Fig. 5) with Scotch tape, and a few feet of 16-mm film were exposed, usually 15 frames per minute. During this prebombardment photography, the portion of the cell to be irradiated was

[4] We have found these locators useful in many other laboratory procedures, for instance, in finding the same bombarded cell repeatedly in histological and polarization studies.

[5] Exploratory experiments have also been performed on cultured cells of warm-blooded animals and on various simple plant and animal forms.

brought accurately beneath the aiming cross hairs by means of the mechanical stage of the adjustable locator. The exact location of the bombardment region was thus permanently and quickly recorded.

Concurrently with selection and prebombardment photography of the cell, the rate at which protons were coming through the microaperture was determined. This was done with a Geiger-Müller counter (*F*, Fig. 6) which could be readily and reproducibly swung into position below the microaperture. The counter had an efficiency of about 100 per cent as determined by alternately bombarding it and Ilford C2 nuclear plates, and was corrected for natural background and for a low count due to Bremsstrahlung produced by protons impinging on the slit jaws. When a suitable rate had been established (usually a few hundred protons per minute), the time required to deliver the desired number of protons was calculated, the counter was swung out of position, the locator with the culture was transferred from the observation microscope to the bombardment stage (Fig. 6), and the latter was raised until the mica cover slip of the culture was about 5 μ from the lower slit jaws. This close approach was accomplished, rapidly and without danger of collision with the precisely adjusted microaperture, by use of a suitable height indicator (*I*, Fig. 6) which had been adjusted beforehand for the particular locator and culture chamber being used. The desired exposure was then given by opening and closing a shutter (not illustrated) in the delivery tube of the proton generator.

The locator was then transferred from the bombardment stage back to the observation microscope (Fig. 5), and the location of the object aimed at was carefully checked against the cross hairs. If, as seldom happened, the "return" was not precise, this was due to faulty seating of the locator or, more likely, to the cell having moved. In either case, the deviation from aiming was carefully noted and the experiment was either discarded or the conclusions drawn from it were restricted in accordance with the extent and direction of the deviation. If the "return" was precise, it was assumed that the protons had been delivered as aimed, because, if either the locator or the cell produced a deviation, it appears highly improbable that an exactly compensating deviation, both in direction and extent, should have occurred.

As soon as the "return" had been checked, time-lapse photography was resumed at a suitable frequency and was continued, supplemented by long-hand notations and diagrams in the cell's individual protocol, until all events of interest had occurred or until observation had to be discontinued for other reasons.

It is clear that the foregoing bombardment method is applicable to any cell (or other microscopic object) which can be brought close to the microaperture, which does not move or can be immobilized during bombardment, and in which suitable microscopic targets can be seen in the living condition.

Observations

Observations to date have been preponderantly on cells irradiated in various phases of mitosis. As background for interpretation of the results of partial-cell irradiation, some 250 cells have been totally x-irradiated with from 50 to 4000 r. The following well-known qualitative effects have been observed and recorded: (1) temporary chromosome bridges (duration, 6 hr or less); (2) permanent chromosome bridges (if they last more than 6 hr, they usually persist for days); (3) inhibition of anaphase movement at various stages in the process; (4) complete inhibition of anaphase; (5) inhibition of metaphase configuration (if irradiated in prophase); (6) inhibition of cytoplasmic constriction (cleavage); (7) displacement of constriction with respect to chromosomes; (8) unequal distribution of chromosomes between daughter nuclei because of abnormal anaphase movement and/or misplaced constriction; (9) interference with reconstruction of daughter nuclei; (10) rapid and repeated protrusion of abnormally large cytoplasmic "bubbles," usually beginning about the time of cell constriction. The first four of these effects

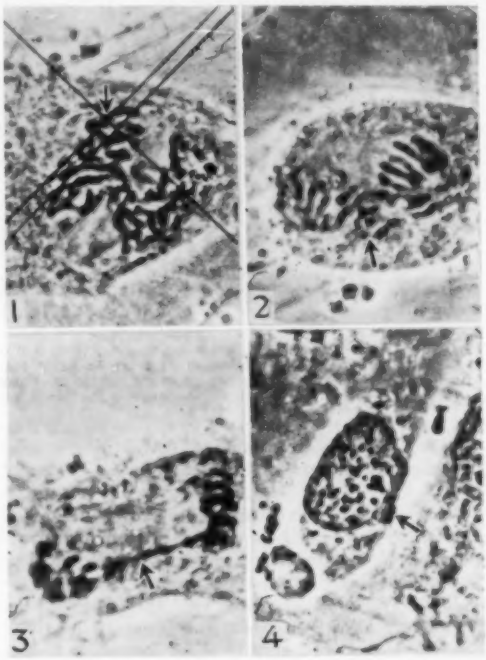

Fig. 8. Anaphase hinge. (Prints from 16-mm motion-picture film.) (1) Cell at time of bombardment. Place marked by arrow. (2) Chromosome groups form 90° hinge in anaphase because of bridge (arrow) produced by bombarded chromosomes. (3) Bridge (arrow) persists as hinge straightens out. (4) Bridge has broken, and small accessory nucleus (arrow) appears beside one of the large daughter nuclei. (Area shown in each frame is 45 × 60 μ.)

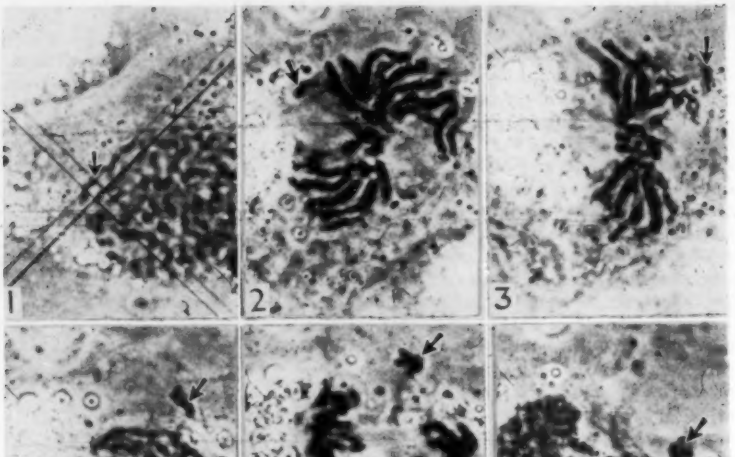

FIG. 9. Development of an accessory nucleus. (Prints from 16-mm motion-picture film.) (1) Bombardment (arrow). (2) Position of bombarded chromosomes (arrow) in early metaphase. (3–5) A chromatin clump consisting of one or more chromosomes (arrows) is detached from the rest of the chromosome group. (6) Membrane (arrow) has formed around this clump. Two other accessory nuclei lie between the two large nuclei. (Area shown in each frame is 45 × 60 μ.)

were smoothly dose-dependent.[6] A few dozen cells have been totally proton-irradiated, with similar results.

In some 120 nonirradiated cells, most of these abnormalities have not been observed at all. Two temporary and one permanent bridge occurred, and a few cells "bubbled" as specified in item 10 above.

In 300 partially irradiated cells the same qualitative effects have been observed. However, the chromosome aberrations were localized according to the spot of bombardment. A few dozen[7] protons through the middle of a metaphase plate or of a prophase chromosome configuration regularly produced bridges; a few hundred protons produced so many bridges that anaphase was stopped early. A few dozen protons to one corner of the "butterfly" configuration in metaphase (Fig. 8) regularly produced a bridge near one side of the spindle; if the bridge was strong enough, its tension and the normal forces of anaphase movement (whatever they may be) produced an anaphase "hinge" (2, Fig. 8).

[6] We shall describe in another place the dependence of these effects on dose, stage of mitosis, irradiation, etc., as well as modification of the mitotic time schedule.

[7] Partial-cell bombardments are here stated as numbers of individual protons which traverse the cell part. In partial-cell irradiation the concept of dose (energy transferred per unit mass of cell) is complicated and will be discussed elsewhere.

Although even a few dozen protons to the chromosomes[8] regularly produced unambiguous abnormalities (chiefly bridges), hundreds and even a few thousands to extrachromosomal regions (general cytoplasm, spindle, centriolar region) produced no detectable effects, if no more than a few protons were scattered into the chromosomes.

Occasionally it was possible, because of an outspread configuration of the chromosomes in early metaphase, to bombard a single chromosome with fair selectivity and produce nondisjunction of the two daughter chromosomes, both going to the same pole in anaphase.

As a result of partial-cell irradiation, small accessory nuclei (sometimes called "micronuclei") were frequently produced (4, Fig. 8), although this has never been unequivocally observed in our totally irradiated cells.[9] Usually these accessory nuclei appeared late, presumably having been obscured previously by the large neighboring nucleus. However, in one case we traced the full development of one of several accessory nuclei that resulted from the localized irradiation of a few chromosomes in prophase. A few frames from the motion picture are shown in Fig. 9.

[8] Of course, in chromosome bombardments a small amount of cytoplasm was also irradiated.

[9] In some material, accessory nuclei are copious after total-cell irradiation (e.g., Politzer, *12*).

Details of the observations and also of the apparatus will be published elsewhere.

A widely applicable method has been developed for high-energy irradiation of cell parts by use of proton microbeams with diameters as small as 2.5 μ. In mitotic cells of newt heart cultures, a few dozen protons to chromosomes produce severe aberrations, whereas a few thousand to cytoplasm, spindle, or centriolar region are without detectable effect. Some of these types of chromosome aberrations are readily localized and help in the study of certain aspects of mitotic movement.

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News and Notes

Southern Society of Cancer Cytology

January 25th marked the second meeting of the Southern Society of Cancer Cytology, the inaugural meeting having taken place in Miami last November during the Southern Medical Association meeting. The 88 members in this group represent 13 of the southern states and the District of Columbia, and include many leading clinicians, cytologists, pathologists, and researchers, all having a special interest in cancer cytology.

The aims of the organization, as set forth in the by-laws, are as follows:

1. To stimulate the development of standards of nomenclature, cell classification, techniques, education, etc.
2. To stimulate research, both practical and theoretical, on problems related to cancer.
3. To stimulate education in cancer cytology.
4. To provide a forum for discussion of cytological problems.
5. To promote sound statistical studies based on uniform and standard methods.
6. To act as a regional advisory group covering the aforementioned objectives.

Honorary members of the society include the following: Emil Novak, Herbert F. Traut, Charles Read, Wilton R. Earle, Edgar R. Pund, and Robert Chambers.

The following officers were elected to serve for two years from the date of the inaugural meeting: president, F. Bayard Carter; vice president, M. Y. Dabney; secretary, J. Ernest Ayre; treasurer, Joseph K. Cline.

This new society is organized around three councils and two committees, which include:

Pathology Advisory Council: C. C. Erickson, chairman, associate director, Institute of Pathology, University of Tennessee; Virgil H. Moon, professor of pathology, University of Miami; J. M. Blumberg, pathologist, Walter Reed Army Hospital, Washington, D. C.; Paul Kimmelstiel, pathologist, Charlotte Memorial Hospital, Charlotte, N. C.

Clinical Advisory Council: F. Bayard Carter, chairman, head, Department of Obstetrics and Gynecology, Duke University, Durham, N. C.; Ralph W. Jack, Miami, Florida; M. Y. Dabney, editor, *Southern Medical Journal*; John E. Dunn, chief, Field Investigation Center Cancer Control Branch, National Cancer Institute; R. W. TeLinde, Johns Hopkins Hospital, Baltimore, Md.

Cytology Advisory Council: J. Ernest Ayre, chairman, director, Dade County Cancer Institute, Miami, Florida; Robert E. Seibels, Columbia, South Carolina; H. E. Nieburgs, Department of Clinical Cytology, Medical College of Georgia, Augusta; L. I. Platt, Washington, D. C.; E. E. Siegler, U. S. Public Health Service, Memphis, Tenn.

Research Advisory Committee: J. K. Cline, chairman, director of cancer research, Medical College of Alabama, Birmingham.

Educational Advisory Committee: Homer L. Pearson, chairman, Miami, Fla.; Jay F. W. Pearson, president, University of Miami, Fla.; Chauncey Leake, vice president, University of Texas Medical Branch.

This group is planning to hold the first scientific session at Atlanta, Ga., in November of this year, simultaneously with the sessions of the Southern Medical Association. Application is being made by this society to cooperate in establishing a Section on Cytology of the Southern Medical Association.

Regular membership in the society is open to physicians, scientists and other research workers, interested in the furthering of cytology, and associate membership is open to technicians in the field. The territorial scope of the Southern Society of Cancer Cytology includes the states covered by the Southern Medical Association.

J. Ernest Ayre

Dade County Cancer Institute, Miami, Florida

Scientists in the News

Erwin H. Ackerknecht, professor of the history of medicine, University of Wisconsin Medical School, has been awarded the William H. Welch Medal of the American Association of the History of Medicine, for work in the field of medical history.

R. A. Alexander, director of Veterinary Services for the Union of South Africa, has arrived in Washington, D. C., at the invitation of the U. S. Department of Agriculture, to assist in a study of the sheep disease known as blue-tongue. Dr. Alexander will make field investigations in California, Texas and Utah, the states in which symptoms of the disease have been reported.

C. C. Carpenter, dean of the Bowman Gray School of Medicine of Wake Forest College, N. C., has been awarded a Fulbright visiting professorship in pathology for a nine months' lecture series in Cairo, Egypt. He will lecture at the Ibrahin Pasha University Medical School and the medical college of the University of Cairo.

Earl S. Ebers, formerly sales manager of Kralastic and Vibrin resins, Naugatuck Chemical Division, United States Rubber Company, has been named director of research and development of the division, to replace **M. G. Shepard,** who has retired. **Lorin Schoene,** formerly manager of plastics development, was appointed assistant director of research and development.

John F. Enders, associate professor of bacteriology at Harvard Medical School, will receive the 1953 Passano Foundation Award in recognition of work on the culturing of poliomyelitis viruses in tissue.

Richard B. Goldschmidt, geneticist and emeritus professor of zoology on the Berkeley campus of the University of California, recently received two science honors from Free Germany on the occasion of his 75th birthday. Dr. Goldschmidt was made an honorary member of the German Zoological Society, and received an honorary degree of Doctor of Natural Sciences from the Free University of Berlin. He was director of the Kaiser Wilhelm Institute for 15 years before coming to this country in 1936.

Emmette F. Izard, of the Du Pont Company, Buffalo, N. Y., has won the 1953 Jacob F. Schoellkopf Medal of the American Chemical Society's Western New York Section. Dr. Izard was cited for his discovery of polyethelene terephthalate—a material also discovered independently by **J. R. Whinfield,** of the British Calico Printers Association—and for contributions to the development of a process for converting it into finished fibers and films.

J. Lanjouw, director of the Botanical Museum of the University of Utrecht, and secretary of the newly established International Association of Plant Taxonomists, has arrived in the U.S. to visit several botanical museums. Dr. Lanjouw will consult with colleagues about the program of the International Bureau of Plant Taxonomy and Nomenclature, particularly in connection with nomenclature sessions of the Eighth International Botanical Congress, to be held in Paris in 1954. He will also lecture on the vegetation of Surinam at several American universities.

Gillie A. Larew, dean of Randolph-Macon Woman's College, will retire at the end of the summer after more than 50 years' association with the college as student, faculty member in the Department of Mathematics, and dean.

B. D. McDaniel, of the Nuclear Physics Department, Cornell University, has arrived in Canberra, where he will join the Nuclear Physics Department of the Australian National University. He is on a Fulbright Fellowship, and will be in Australia nearly a year.

Raymond W. McNamee, superintendent of the Research and Development Department of the Carbide and Carbon Chemicals Company, South Charleston, W. Va., has been chosen by the American Chemical Society's Georgia Section to receive the 1953 Herty Medal, given for contributions to chemistry in the Southeast.

Glenn A. Noble, head of the Department of Biology, California State Polytechnic College, San Luis Obispo, Calif., has been selected by the Board of Foreign Scholarships to receive a Fulbright award. Dr. Noble will leave at the end of the spring quarter for Manila, where he will lecture in veterinary parasitology at the University of the Philippines.

Eugene P. Pendergrass, head of the Department of Radiology, University of Pennsylvania School of Medicine, received the fifth annual award of the American Cancer Society for service in the field of cancer control. Dr. Pendergrass was honored for research in radiology, and for diagnosis of deep-seated cancer by means of x-ray.

A. C. Smith, Smithsonian Institution botanist, will collect plants in the Fiji Islands during the next nine months. This will be Dr. Smith's third Fijian expedition, his first and second trips having been made for the Arnold Arboretum of Harvard University in 1933 and 1947. Aside from their intrinsic botanical interest, Fijian plants are indicators of ancient land connections in the South Pacific.

Edward Teller, professor of physics at the University of Chicago, has been appointed professor of physics, University of California, Berkeley, effective July 1. Dr. Teller is now on leave of absence, working in the Radiation Laboratory at Berkeley, and will continue part-time in such work.

W. L. Waterhouse has received the James Cook Medal of the Royal Society of New South Wales, an award made for contributions to science and human welfare in and for the Southern Hemisphere.

Education

Two special institutes for teachers of college and high school physics will be conducted at the **University of Minnesota** during the first summer session, June 15–July 17. The high school teachers' institute will be divided into four phases: demonstration lectures in classical physics—basic concepts and principles; an introduction to present-day physics research through lectures and visits to university and industrial laboratories in the Twin Cities; discussions on the relation of physics to other sciences such as botany and zoology; and joint meetings with the college teachers to talk over coordination with college physics. The institute for college physics teachers has been designed to bring participants in close touch with current research at the university and elsewhere. Lecturers and their subjects will be: J. H. Williams on experiments with the Van de Graaff generator; E. P. Ney and J. R. Winkler on cosmic rays; O. H. Schmitt on biophysics; A. J. Dekker on thermonic emission and related topics; and A. O. C. Nier on mass spectroscopy. In a parallel series of lectures, E. L. Hill will cover magnetism of matter in bulk; W. H. Brattain of Bell Telephone Laboratories will talk on transistors and semi-conductors; and G. E. Pake of Washington University will lecture on magnetic resonance and related phenomena. Supported by the Ford Foundation's Fund for the Advancement of Education, approximately 30 scholarships, covering all cost of the institute plus transportation and living expenses, will be awarded to high school physics teachers. The other institute, made possible by a grant from the National Science Foundation, will provide similar scholarships for approximately 20 college physics teachers. Recipients will receive stipends for all tuition and laboratory fees, board, room, books, and travel in connection with the institute.

West Virginia University will again operate its general summer field courses in botany and zoology, June 7–July 14, from a permanent base at Camp Arthur Wood, the university's forestry camp near Alvon in Greenbrier County. Leland H. Taylor and Herald D. Bennett will be directors of the courses, and applications should be received by *May 15*.

Meetings and Elections

The **Second International Congress on Rheology** will be held at Oxford University, July 26–31. In addition to contributed papers, the general lectures include: the presidential address, "Rheology for Mathematicians," by Geoffrey Taylor, of Cambridge; "Sur l'effet électrovisqueux," by Mme. A. Dobry Duclaux, Paris; "Rheological Problems in the Fabrication of Plastics," by R. S. Spencer, Midland, Mich.; "Rheology and Applied Mechanics," by R. N. J. Saal, Amsterdam; "Rheological Behaviour and the Molecular Jumping Mechanism," F. H. Müller, Marburg; "Water Association and Hydrogels," E. Forslind, Stockholm; and "Biological Problems for the Rheologist," P. Eggleton, Edinburgh.

The fourth **Symposium on Plasticity** will be held at Brown University, Sept. 1–3. The three principal topics of this symposium will be: stress-strain relations (perfectly plastic, work-hardening, visco-elastic, and visco-plastic materials); distribution of stress and strain in bodies exhibiting inelastic properties (static and dynamic problems, infinitesimal and finite deformations); and structural analysis and design in the inelastic range (limit analysis, static and dynamic loading, shakedown, inelastic buckling). Foreign and American experts in the field will present research papers, and everyone is invited to participate in the discussion. Certain sessions of the symposium of particular interest to civil engineers are being sponsored, jointly with Brown University, by the Engineering Mechanics Division of the American Society of Civil Engineers. The remaining sessions are under the joint sponsorship of the Office of Naval Research and Brown University. All persons interested in receiving further information concerning the symposium should write to Prof. H. J. Weiss, Graduate Division, Brown University, Providence 12, R. I.

Miscellaneous

The **International Society for the Welfare of Cripples,** 127 E. 52nd St., New York City, has announced the establishment of the Irving Geist International Film Library. The library will make films concerned with rehabilitation available to groups all over the world. Information may be secured from the society. Affiliated organizations and members of its United States Committee may borrow films without charge. A service fee of $2.00 will be made to others.

The **National Research Council** recently approved the establishment of a Committee on Clay Minerals to coordinate work being done in clay mineralogy and to bring together workers in the various allied fields. The new committee has been set up under the Division of Geology and Geography, with representatives from the Divisions of Biology and Agriculture and of Chemistry and Chemical Technology. Chairman of the committee will be Ralph E. Grim of the University of Illinois.

The **Scientific Manpower Commission,** recently organized by eight major scientific societies, has opened an office in Washington at 1530 P Street, N.W., and has embarked upon a broad program designed to assure the nation of an adequate supply of scientists. Dr. Howard A. Meyerhoff, formerly administrative secretary of the American Association for the Advancement of Science, is president of the commission.

Sixteen scientists, nominated by the participating societies, will make up the commission, which will study the nation's needs for scientists in education, industry, government service and the armed forces, and will direct its efforts toward bringing the scientific

manpower supply and demand into adjustment under changing international economic conditions.

Other officers of the commission are E. G. Begle of Yale University, vice-president, and Milton O. Lee, of the Federation of American Societies for Experimental Biology, secretary-treasurer. Other members are: Henry A. Barton, American Institute of Physics; Detlev W. Bronk, National Academy of Sciences; Stewart S. Cairns, University of Illinois; Leonard Carmichael, Smithsonian Institution; M. T. Carpenter, Standard Oil Company of Indiana; Frank P. Cullinan, U. S. Department of Agriculture; George R. Harrison, Massachusetts Institute of Technology; John S. Nicholas, Yale University; Joseph H. Roe, George Washington University; B. R. Stanerson, American Chemical Society; and Dael Wolfle, Commission on Human Resources, National Research Council.

Incorporated in the District of Columbia, the Scientific Manpower Commission was established through the cooperation of the American Association for the Advancement of Science, American Chemical Society, American Geological Institute, American Institute of Biological Sciences, American Institute of Physics, American Psychological Association, Federation of American Societies for Experimental Biology, and the Liaison Committee of the Mathematical Societies. Other private scientific societies will presumably work through the commission now that it is organized.

Recent Deaths

Henry J. Althenn (62), mathematician, Elizabeth, N. J., March 30; **John L. Ames** (90), physician, Larchmont, N. Y., March 20; **Jacob P. Anderson** (78), botanist, Ames, Ia., Feb. 13; **Rose Bass** (50), gynecologist and endocrinologist, East Orange, N. J., Apr. 15; **Frederick W. Beckett** (84), engineer, Syracuse, N. Y., March 22; **Charles B. Bohn** (73), of Detroit, industrialist, Miami, Fla., Apr. 2; **William P. Brandes** (68), of New York, engineer, Doylestown, Pa., Apr. 8; **Henry A. Bunker** (63), psychiatrist, New York, N. Y., March 19; **Pierce Butler** (66), of Chicago, educator, Chapel Hill, N. C., March 26; **Augustus Camprubi** (63), consulting engineer, Jackson Heights, Queens, N. Y., Apr. 15; **Richard N. Connolly** (90), pathologist, Newark N. J., March 25; **Robert L. De Normandie** (78), obstetrician, Woodstock, Vt., Apr. 20; **John T. H. Dempster** (85), original staff of GE Research Laboratory, Schenectady, N. Y., Apr. 5; **Blanche C. Downie** (60), hygienist, Philadelphia, Pa., March 24; **Louis W. Downes** (87), electrical engineer, Providence, R. I., Apr. 7; **Gano Dunn** (82), engineer and industrialist, New York, N. Y., Apr. 10; **George B. Ebersole** (60), mechanical engineer, Westfield, N. J., Apr. 3; **Frederick W. Eldridge-Green** (89), ophthalmologist and color and vision specialist, Worthing, England, April 17; **Charles W. Engle** (—), engineer, Cleveland, Ohio, March 19; **John N. Evans** (—), ophthalmologist, Brooklyn, N. Y., Apr. 8.

Samuel Feigin (58), psychiatrist, of New York, N. Y., Palm Beach, Fla., Mar. 20; **Harold A. Foster** (71), of New York, N. Y., Montclair, N. J., Apr. 5; **Emanuel A. Goldenweiser** (69), economist, Princeton, N. J., March 31; **Gerald Gould** (63), fuel engineer, Wilton, Conn., March 20; **Andrew Gray** (80), radio pioneer, London, Eng., March 22; **Alice Gregory** (77), surgeon, New York, N. Y., Apr. 20; **Ronald W. Gurney** (54), physical chemist, New York, N. Y., Apr. 14; **William S. Hadaway** (87), electrical engineer, Bound Brook, N. J., Apr. 12; **Frederick S. Hammett** (58), radiologist, New York, N. Y., Apr. 7; **Clinton H. Havill** (60), research engineer, East Orange, N. J., March 25; **George S. Hodges** (89), inventor, Pine Lake, Mich., Apr. 11; **George H. Humphreys** (76), Queens, N. Y., Apr. 16; **Charles J. Jones** (86), ophthalmologist, Philadelphia, Pa., Apr. 15; **C. E. M. Joad** (61), philosopher, London, Eng., Apr. 9; **Boris Kidric** (40), Yugoslavian economist, Belgrade, Yugoslavia, Apr. 11; **Frederick A. Kiehle** (80), eye specialist, Palo Alto, Calif., March 22; **John W. Kissane** (74), pediatrician, Malone, N. Y., Apr. 2; **Charles R. Knight** (78), museum artist, New York, N. Y., Apr. 15; **Alois Kraus** (90), of Germany, economic geographer, Bryn Mawr, Pa., March 31; **Anna R. Lapham** (83), physician, Chicago, March 31; **Marvin L. Latimer** (46), physician and professor of clinical medicine, New Haven, Conn., Apr. 17; **Robert D. Laurie** (78), of Wales, zoologist, Amsterdam, Apr. 7; **Eugene R. Lewis** (75), professor of surgery, Los Angeles, March 18; **Edward K. Love** (83), conservationist, St. Louis, Mo., March 22; **Dean S. Luce** (77), Canton, Mass., Apr. 9.

John J. MacDonald (80), skin specialist, Jersey City, N. J., Apr. 6; **Henry A. Mattill** (69), biochemist, Iowa City, Ia., March 30; **Charles Modica** (50), physician, New York, N. Y., Apr. 4; **Enrique Moles** (69), atomic physicist, Madrid, Spain, March 30; **Lewis F. Moody** (73), professor and hydraulic engineer, Plainfield, N. J., Apr. 18; **George E. Morton** (47), electronics engineer, Cleveland, Ohio, Apr. 8; **John C. Parker** (73), electrical engineer and industrialist, March 23; **Joel B. Peterson** (55), physician, Summit, N. J., March 30; **Jacob Pulenskey** (82), electrical engineer, Watervliet, N. Y., Apr. 8; **Frank Purnell** (66), industrialist, Youngstown, Ohio, Apr. 19; **Elizabeth Ross** (—), of Pittsburgh, pathologist, Pictou, Nova Scotia, Apr. 16; **Arseni Vasilevich Rusakov** (—), specialist in forensic medicine, Moscow, U.S.S.R.; **George Sandalls, Jr.** (55), electrical engineer, North Tarrytown, N. Y., March 30; **Arkadii Dmitrievich Shvetsov** (—), aviation designer, Moscow, U.S.S.R., March 19; **D. C. Thurman, Jr.** (—), of Washington, D. C., Thailand Apr. 17; **John K. Toole** (57), urological surgeon, Branford, Conn., Apr. 19; **Edward J. Turbert** (—), physician, West Hartford, Conn., Apr. 3: **Phillip Van Ingen** (77), pediatrician, New York, N. Y., March 31; **Charles F. Vaughn** (78), research engineer, Niagara Falls, N. Y., March 30; **Francis M. Walters** (65), physical metallurgist, Los Alamos, N. M., Apr. 18; **Morris Weintrob** (52), surgeon, Brooklyn, Apr. 7.

Technical Papers

Effect of 3-Chloro-Isopropyl-N-Phenyl Carbamate on Abscission of Young Fruits of Peach

Paul C. Marth and Victor E. Prince

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Peach thinning experiments with sprays containing 3-chloro-isopropyl-N-phenyl carbamate (3-Cl-IPC) conducted during the 1952 season indicate that this compound offers promise as a new thinning agent. These preliminary results are believed to be of sufficient interest to warrant further trials of this and related carbamates for thinning peaches. The need for a reliable chemical thinning agent for peaches is shown by the work of other investigators (*1, 2*).

In the present experiments peach trees that had currently set a heavy crop were used. Two adjacent branches of approximately equal size on each tree were used; one received the spray while the other served as the control. Afterglow and Hiley varieties were sprayed with 200 ppm aqueous concentration of 3-Cl-IPC on May 16, 1952, approximately 30 days after full bloom; Halehaven, Laterose, Raritan Rose, and Triogem peaches, and Flaming Gold nectarines were sprayed with a 500 ppm concentration on May 28, approximately 42 days after full bloom. Technical grade 3-Cl-IPC was dispersed in water by dissolving it in Tween 20, used at 0.5% in all sprays. A 3-gal pressure sprayer was used to wet all parts of the branches thoroughly with the sprays. Pressure tests to determine maturity of fruits were made with a Magness-Taylor pressure tester fitted with a 5/16-in. plunger.

Fruit thinning effects were evident on sprayed branches of Afterglow and Hiley varieties one week after treatment (200 ppm 3-Cl-IPC applied 30 days after full bloom), when many treated fruits were shriveling. At this time the effect of the spray seemed too severe and the concentration too great. Records at harvest showed that this was the case (Table 1). Hiley fruits were drastically overthinned by the spray, only 18% of the original number being on the tree at harvest. Natural thinning during the June drop reduced the drop of this variety to about the optimum (46% at harvest) on the control limb. The variety Afterglow also was overthinned by the chemical.

Application of 3-Cl-IPC at 500 ppm concentration approximately 42 days after full bloom caused about half of the fruits of Laterose, Raritan Rose, and Triogem varieties to abscise, leaving what appeared to be about the optimum numbers for the limbs to bear (Table 1). Halehaven peach lost 39% of its crop through natural causes, and the spray thinned the crop even further so that only 36% of the fruits remained on the tree at harvest. Flaming Gold nectarine also was overthinned by the spray. At harvest, fruits of all varieties except Halehaven averaged larger on sprayed branches than on unsprayed ones. Pressure tests at that time showed that the treated fruits matured earlier and were softer than the controls (Table 1).

TABLE 1

FRUIT THINNING INDUCED BY SPRAY APPLICATION OF 3-CHLORO-ISOPROPYL-N-PHENYL CARBAMATE (3-Cl-IPC) TO INDIVIDUAL BRANCHES OF 6 VARIETIES OF PEACH AND 1 VARIETY OF NECTARINE

Variety	Treatment	No. of fruits present at start	Percentage remaining at harvest	Av size of fruit (mm)	Av pressure-test reading (firmness [lb])
Afterglow	Control	122	76	202	15.8
	3-Cl-IPC*	145	37	227	9.5
Halehaven	Control	38	61	175	21.3
	3-Cl-IPC†	64	36	177	7.5
Hiley	Control	136	46	191	10.2
	3-Cl-IPC*	101	18	204	9.5
Laterose	Control	102	92	186	9.3
	3-Cl-IPC†	256	52	210	5.4
Raritan Rose	Control	121	83	174	13.1
	3-Cl-IPC†	165	50	193	3.0
Triogem	Control	142	100	159	17.0
	3-Cl-IPC†	128	46	172	14.1
Flaming Gold (nectarine)	Control	140	82	—	—
	3-Cl-IPC†	192	22	—	—

* Applied as an aqueous spray at 200 ppm concentration approximately 30 days after full bloom.

† Applied as an aqueous spray at 500 ppm concentration approximately 42 days after full bloom.

Under the conditions of these experiments young expanding leaves of peach and nectarine showed no apparent discoloration or injury due to the spray applications. In contrast, a thinning spray of naphthalene acetic acid applied at 30 to 40 ppm concentration generally caused moderate to severe epinasty of young developing peach leaves, a week or more being required for recovery.

Certain inherent characteristics of 3-Cl-IPC should be considered in evaluating it further as a thinning agent. At moderately high temperatures the chemical evaporates rather rapidly (*3*); thus the response obtained may vary considerably, depending upon the amount applied and the temperature. Half as much was required to keep potato tubers dormant at 50° to 60° F as at 70° to 75° (*4*). Stage of development may also strongly influence the results, since carbamates affect cell division (*5*). Extensive tests with

carbamates as herbicides indicate that some kinds of plants are more readily affected than others (*6–8*). Preliminary experiments to be reported elsewhere indicate that young fruits of apple are not as sensitive to 3-Cl-IPC as are those of peach.

Although extensive tests on animal toxicity have not been conducted, laboratory tests with small animals carried out by the Industrial Hygiene Foundation of America, Inc., Pittsburgh, Pa., for the Columbia-Southern Chemical Corporation, show that 3-Cl-IPC and the parent carbamate are relatively nontoxic.[1]

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[1] Appreciation is expressed to E. D. Witman of the Columbia-Southern Chemical Corporation, Pittsburgh, Pa., for supplying this information on animal toxicity and the 3-chloro-isopropyl-N-phenyl carbamate used in these studies.

Cells with Metachromatic Cytoplasmic Granules in the Stroma of Human Chorionic Villi

John S. Latta and Charles R. Beber[1]

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In the course of reinvestigating the histological characteristics of the human placenta with the use of various histochemical techniques, certain cells in mesodermal cores of chorionic villi were found to contain metachromatic, eosinophilic granules in their cytoplasm. These seemed to us to be of such interest as to warrant some discussion.

These granular cells were found in the villi of all of 14 placentas examined, ranging in age from 3.5 weeks to term. All material in which they were demonstrable was fixed either in 4% basic lead acetate, or 5% trichloracetic acid, after which paraffin-embedded sections were cut at 5 μ and stained with toluidine blue to demonstrate metachromasia, and with Wright-Giemsa stain to demonstrate eosinophilia. These specific granules were most abundantly demonstrated after basic lead acetate fixation. They were always found in villous stroma but rarely encountered in the basal chorion, placental septa, or amnion.

The granule-bearing cells were quite large, ranging from 12 to 18 μ in diameter. They were generally

[1] C. W. M. Poynter Fellow in the medical sciences.

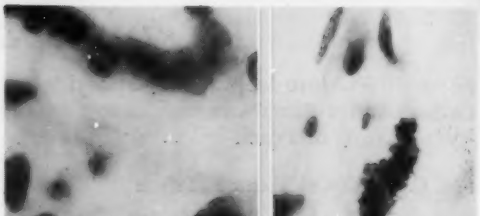

Fig. 1. Portion of a chorionic villus from a term placenta showing two large rounded cells with coarse, eosinophilic cytoplasmic granules in the stroma. Fixation in 4% basic lead acetate, Wright-Giemsa stain. × 1140.

Fig. 2. Villous stroma from a term placenta showing a single cell packed with coarse metachromatic granules. Fixation in 4% basic lead acetate; toluidine blue stain. × 1140.

roughly spherical in shape (Fig. 1) but in many cases exhibited long processes (Fig. 2). The cell membranes quite indistinct, the limits of the cytoplasm being frequently demarcated by the contained granules (Figs. 1–4). The intergranular cytoplasm sometimes seemed to exhibit metachromasia, which was thought to be due to solubility of the granules. The nuclei were spherical or bean-shaped and homogeneously basophilic, on which background were superim-

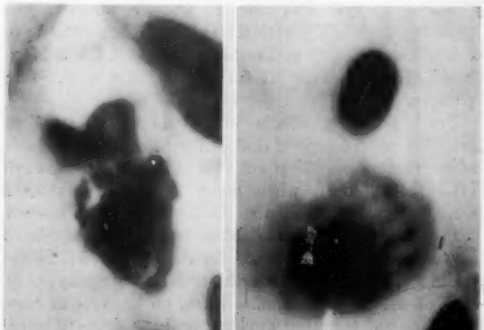

Fig. 3. The surface trophoblast and underlying stroma from a term placenta with a large cell containing very coarse eosinophilic cytoplasmic granules and a condensed diffusely stained nucleus. Fixation in 4% basic lead acetate; Wright-Giemsa stain. × 2190.

Fig. 4. Another large cell in a villus from a placenta of 6 weeks, containing numerous coarse cytoplasmic granules, which stained metachromatically with toluidine blue. Some cytoplasmic metachromasia is apparent. Fixation with 4% basic lead acetate. × 2190.

posed clumped chromatin granules. No nucleoli were observed. These nuclear and cytoplasmic features made the cells easily distinguishable from Hofbauer or phagocytic cells.

The specific granules were quite soluble with routine fixation, although some granules were seen streaming out into the villous stroma and apparently dissolving. With the special fixatives the number per cell varied from 10 to 12 to huge numbers densely packed in the cytoplasm, obscuring the nucleus (Fig. 2). These variations may be real or the result of difficulties of fixation. In all material fixed in basic lead acetate the granules were eosinophilic after Wright-Giemsa or azur II-eosin staining and metachromatic after toluidine blue, but remained unstained after methyl green-pyronin.

The constancy of their presence in chorionic villi of placentae of such widely varied stages and their consistent staining qualities after certain fixatives led to the conclusion that these granule-bearing cells may represent an important feature of the histological structure of the chorionic villus. The eosinophilic staining quality and constancy in size and shape of the granules make it highly improbable that they represent phagocytized material. Cells with such metachromatic granules have been reported in the endometrium and myometrium of the bat uterus by Wimsatt (*1*) and by Asplund and Holmgren (*2*) in human uterine mucosa. The latter authors found them only during the fertile period and varying with the stage of the menstrual cycle. They found them rarely during estrogenic stimulation, but in increasing numbers during progestational stimulation, with a premenstrual peak. They apparently disappeared with the menses.

A recent contribution by Pescetto (*3*) describes cells with metachromatic and basophilic granules in placental tissue after 4% basic lead acetate. His figures indicate a marked resemblance to the cells we describe except for the basophilic reaction of the granules he reported and the age range in which he found them.

Although further chemical assay of these granules has not been attempted, it may be pointed out that Sylvén (*4*) in studies of mast cells has demonstrated that heparin is manufactured as a lipoprotein complex in such cells, and that heparin is metachromatic and eosinophilic. It might be suggested that the cellular granules we have described represent heparin or heparinoid substances to be associated with incoagulable, free-flowing blood in such locations where one might assume it would clot. Such granule-bearing cells have been reported only in uterine mucosa (*1, 2*).

The granules we have studied fail to stain with pyronin in Taft's (*5*) method for nuclear protein and are not destroyed by ribonuclease. The special fixers required for their preservation indicate that they are not a mucopolysaccharide.

It is interesting to note that current therapy as used by Rumbolz, Moon, and Novelli (*6*) in certain types of abnormal uterine bleeding involves intravenous introduction of toluidine blue or protamine sulfate, both of which are known to inactivate heparin. The most striking feature of the cytoplasmic granules we have described is the intensity with which they stain with toluidine blue.

We would suggest then that the metachromatic eosinophilic granules consist of heparin or heparinoid substances that normally are related to the function of maintenance of incoagulable blood in the intervillous spaces of the placenta.

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Effect of Salicylic Acid on the Hypoprothrombinemia Induced by Dicumarol in the Dog and the Rat[1]

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Salicylic acid readily induces a hypoprothrombinemia in the rat (*1*) and augments the hypoprothrombinemia induced by Dicumarol[3] (*2*) in the dog. The purpose of this report is to show that under specified experimental conditions, salicylic acid may actually *reduce* the hypoprothrombinemic response of Dicumarol in the dog as well as in the rat, and prolong the survival time of rats receiving the anticoagulant continuously.

The details of the animal experiments and of the modified one-stage prothrombin assay have already been given in detail (*1–4*). In control studies not included here, the prothrombin time of whole plasma (100%) and of the 50, 25, and 6.25% dilutions was measured. As before, the data will be restricted to the prothrombin time of 12.5% plasma (1 part oxalated plasma, 7 parts saline solution) for reasons emphasized in (*5*).

Acetylsalicylic acid[4] will increase and prolong the

[1] Published with the approval of the director of the Wisconsin Agricultural Experiment Station. Abstracted from a thesis submitted by John B. Field to the Graduate Faculty of the University of Wisconsin in partial fulfillment of the requirements for the Ph.D. degree, May 1944. This work was supported through special grants from the Graduate Research Committee of the university.

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[3] Dicumarol is the trademark for the anticoagulant 3,3'-methylenebis (4-hydroxycoumarin).

[4] Acetylsalicylic acid (aspirin) caused the most drastic hypoprothrombinemia of a large number of salicylate compounds tested in the rat (*6*).

hypoprothrombinemia induced by Dicumarol in the dog (*2*). This effect was readily reproducible when the acetylsalicylic acid was given *after* the anticoagulant and a hypoprothrombinemia had become detectable. This was also true when doses of acetylsalicylic acid up to 100 mg/kg were given simultaneously *with* the anticoagulant (*2*). As noted here for the first time, however, when 1 g/kg of acetylsalicylic acid was given per os *with* the anticoagulant, not only was the hypoprothrombinemic effect of the anticoagulant partially or completely suppressed, but, for several days following, a transitory hyperprothrombinemia could be detected.[5] This response was not obtained solely with the use of huge doses of acetylsalicylic acid. By feeding 10 or 100 mg/kg of the salicylate daily for 7 days prior to the administration of the anticoagulant, a marked reduction in the extent and duration of the hypoprothrombinemia evoked by the anticoagulant alone was observed. Representative results from some thirty trials are given in Table 1.

mg acetylsalicylic acid was added to the ration in combination with the anticoagulant, the average survival of 6 rats was 22 (7–58) days. With a daily intake of 80 mg of acetylsalicylic acid the survival time was 19 (9–26) days (6 rats).

A comparative study was made of the hypothrombinemic plasmas obtained from dogs and rats given either Dicumarol or acetylsalicylic acid. The clotting times of the mixed plasma (undiluted, or diluted to 12.5%) were the mean of the two component plasmas, suggesting that the hypoprothrombinemia evoked by the anticoagulant and salicylic acid affect the same or similar fractions of prothrombin (*7*). These studies were previously reported from this laboratory in (*6*).

That 3,3′-methylenebis(4-hydroxycoumarin) in relatively minute, and salicylates in relatively massive, quantities induce a hypoprothrombinemia might have been considered coincidental were it not that the anticoagulant and salicylic acid bear a strong synthetic-degradation relationship *in vitro* (*1*). This finding has

TABLE 1

REPRESENTATIVE EFFECTS OF FEEDING ACETYLSALICYLIC ACID PRIOR TO, OR SIMULTANEOUSLY WITH, DICUMAROL ON THE HYPOPROTHROMBINEMIA INDUCED BY THE ANTICOAGULANT*

Dose/kg	Manner of feeding acetylsalicylic acid	Prothrombin time (sec) of 12.5% plasma (after giving anticoagulant)							
		Normal	1 day	2 days	3 days	4 days	5 days	6 days	7 days
15 mg Dicumarol		27	39	67	65	63	39		
" " " + 10 mg salicylate in 8 daily doses	Begun 7 days before Dicumarol	25	40	29	23	23			
10 mg Dicumarol		25	51	96	65	38			
" " " + 100 mg salicylate in 8 daily doses	Begun 7 days before Dicumarol	25	77	25	22				
15 mg Dicumarol		27	44	54	37	26			
" " " + 1 g salicylate in 1 dose	Simultaneously with Dicumarol	22	17	19	18	19			
10 mg Dicumarol		25	38	64	71	59	36		
" " " + 1 g salicylate in 2 daily doses	One day before and simultaneously with Dicumarol	22	38	89	24	20	18	17	21
7.5 mg Dicumarol		25	28	69	28	23			
" " " + 1 g salicylate in 3 daily doses	Simultaneously with Dicumarol and for 2 days thereafter	23	17	20	20	20	19	20	22

* Each line of figures is a series of values obtained with a single animal, the test being performed on the same standardized animal.

The effect of acetylsalicylic acid on the action of the anticoagulant was also tested in the rat. When single oral doses of acetylsalicylic acid, 100 mg or more, were given either with Dicumarol (24 hr before sampling) or 12 hr later, the hypoprothrombinemia induced by the anticoagulant alone was reduced (Table 2). Supplementing anticoagulant-fed rats with salicylates also prolonged their survival time. Thus, control rats maintained on the low vitamin K semisynthetic diet survived a daily intake of 2 mg of the anticoagulant for approximately 13 (5–23) days (*3*). When 10

[5] In other unpublished experiments, we have observed that compounds chemically related to those possessing anticoagulant properties (various coumarin and salicylate derivatives) induced a detectable *hyperprothrombinemia* in trials where they failed to induce a *hypoprothrombinemia* in rats.

sustained the assumption that a similar *in vivo* mechanism operates, although indeed neither has an intermediate compound nor salicylic acid been found in examination of animals given 3,3′-methylenebis(4-hydroxycoumarin) (*6*). More annoying still is the absence of firm evidence pointing to the mechanism whereby both agents affect a hypoprothrombinemia. It is still assumed that there is a suspension of a hepatic synthesis of the protein (*8*).

It has been held that the demonstration of vitamin K inhibition of 3,3′-methylenebis(4-hydroxycoumarin) (*3*) represents a biological antagonism because of a gross similarity in the structure of the two agents producing a competitive phenomenon (*9*). The same phenomenon of competitive inhibition can be drawn upon

TABLE 2

THE EFFECT OF ACETYLSALICYLIC ACID* ON THE HYPOPROTHROMBINEMIA INDUCED IN THE RAT BY FEEDING 2.5 MG DICUMAROL†

Dose of acetylsalicylic acid (mg)	Prothrombin time (sec) of 12.5% plasma		No. of rats
	Acetylsalicylic acid given 12 hr after anticoagulant	Acetylsalicylic acid given with anticoagulant	
None	116 (86–152)	116 (86–152)	365
10	109 (70–150)	113 (100–125)	12
100	87 (60–160)	101 (98–105)	14
200	88 (78–129)	78 (51– 97)	12
300	89 (78–113)	66 (60– 80)	12

* Given by stomach tube in a suspension with 2% gum tragacanth.

† In the standard procedure of this laboratory (*3*), blood samples are removed 24 hr following the administration of the anticoagulant.

to explain vitamin K-salicylate antagonism. The *in vivo* detoxication of salicylates is known to produce a variety of degradation and conjugation products (*10*), a mechanism which conceivably could lead to the accumulation of an agent acting as an inhibitor of coumarin hypoprothrombinemia. Similarly, the evolution of a metabolically derived inhibitor would explain the relative difficulty in inducing hypoprothrombinemia with salicylates. It may be suggested that salicylate detoxication results in a derivative which closely resembles the as yet unknown metabolic derivative(s) of 3,3′-methylenebis(4-hydroxycoumarin) causative of hypoprothrombinemia and as a biological antagonist produces inhibition of hypoprothrombinemia. That the salicylate factor can accumulate in sufficient quantity preceding the administration of the anticoagulant may explain why an inhibition results, whereas a superimposed hypoprothrombinemia develops from administration of salicylates *after* the anticoagulant.

That salicylates can be given to rats *after* coumarin anticoagulant hypoprothrombinemia has been established and still reduce its extent militates against the possibility that salicylates may inhibit Dicumarol absorption, and points up the difference in susceptibility of dogs and rats to the hypoprothrombinemia induced by salicylic acid (*1, 2*). The testing of individual metabolic derivatives of the salicylate molecule in animals given Dicumarol has yet to be done and may prove helpful in elucidating the pathway of coumarin anticoagulants.

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Effects of Soils and Sunlight on Dilute Concentrations of Sodium Pentachlorophenate[1]

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In field trials to determine the effects of potential molluscacides on the snail intermediate hosts of *Schistosoma mansoni*, the human blood fluke in Brazil, variable results were occasionally obtained with a given chemical. The probability of soil being one of the factors that influence the efficacy of molluscacides was indicated by observations that the mortality of snails was usually lower in test plots having a muddy bottom. These observations were further supported by tests showing that concentrations of the pentachlorophenate group of molluscacides decreased most rapidly in test plots having a thick underlying layer of soft mud. With the tests developed by Haskins (*1*), microgram quantities of the molluscacides, copper and sodium pentachlorophenates, were easily determined. Unfortunately, analytical methods for determining other molluscacides in high dilutions were not available.

To exclude other factors that may inactivate molluscacides under field conditions, experiments to determine the effect of various soils on sodium pentachlorophenate were carried on in the laboratory. For the tests, different types of water-saturated soil, taken from waters inhabited by planorbid snails, were packed into 1000-ml beakers at the proportions indicated in Table 1. Each beaker was then filled with a solution having a pH of 7.2 and containing 10 ppm sodium pentachlorophenate. Dried mud was used in Expts. 5 and 6, and in the latter it was mixed with the solution until an opaque suspension was formed. A 10-ppm solution of sodium pentachlorophenate served as a control (No. 9). The room temperature during the period of observation ranged from 27° to 33° C.

The laboratory findings corroborate the field observations in that various earthy materials in some way reduced the concentrations of sodium pentachlorophenate. The greater the depth of the mud in proportion to the depth of the water (Expts. 1–4), the more rapid the decrease. Although the mud used in these experiments came from the same place, similar results were obtained with soils from other sites. In preparation of Expt. 5 the water became cloudy with a suspension of mud, which apparently caused the very rapid diminution in concentration of the chemical. Deliberate stirring of the soil suspension (No. 6) resulted in a reduction to 5 ppm in 1 hr, with only a trace of chemical present 4 hr after treatment. In Expts. 7 and 8 the sandy loam and sand with smaller quantities of

[1] From studies conducted at the Instituto Aggeu Magalhães by the Laboratory of Tropical Diseases of the National Institutes of Health, USPHS, under the sponsorship of the Pan American Sanitary Bureau in cooperation with the Divisão de Organisação Sanitaria do Departamento Nacional de Saude of Brazil.

TABLE 1

CHANGES IN THE CONCENTRATION OF SODIUM PENTACHLOROPHENATE IN LABORATORY EXPERIMENTS WITH VARIOUS TYPES AND AMOUNTS OF SOIL

Time after applying chemical	(No. of expt.) 1	2	3	4	5	6	7	8	9
	(Proportional volumes of solution and soil)								
	Sol. 3 Mud 1	Sol. 1 Mud 1	Sol. 1 Mud 3	Sol. 1 Mud 7	Sol. 1 Dry Mud 1	Sol. 3 Mixed Mud 1	Sol. 1 Loam 3	Sol. 1 Sand 3	Sol. —
	(Concentration in ppm)								
4 hr	10	10	10	10 –	10 –	T*†	10	10	10
21 "	10	10	10 –	5	1	0	10	10	10
29 "	10 –	10 –	5 +	5 –	1	0	10	10 –	10
2 days	10 –	5	5 –	2 –	T	0	10	10 –	10
3 "	10 –	5	2 +	1	T	0	10 –	10 –	10
4 "	5 +	5 –	2 –	T	0	0	5 +	10 –	10
5 "	5	5 –	1	T	0	0	5 –	10 –	10
7 "	5	2 –	T	T	0	0	T	10 –	10
11 "	5 –	2 –	T	0	0	0	T	10 –	10
17 "	2 –	1	0	0	0	0	T	0	10
21 "	2 –	T	0	0	0	0	T	0	10
30 "	1	T	0	0	0	0	0	0	10

* T = Trace of chemical.
† Reduced to 5 ppm in 1 hr.

organic matter and clays had a much less pronounced effect on the concentration of sodium pentachlorophenate. Other conditions being equal, an increased residual effect could be expected after application of chemicals in waters having sandy beds. During a 72-day period all chemical determinations of the control, Expt. 9, were consistently 10 ppm.

Facilities were not available to determine the manner in which silt and clays reduced the concentration of the salts of pentachlorophenol in solution. Presumably the principal process is adsorption of the chemical by the fine particles of soil, but possibly it could be due to actual inorganic or organic chemical combinations, or a coalition of these factors.

To determine the effects of sunlight on dilute solutions of sodium pentachlorophenate, laboratory preparations identical to those in Table 1 were exposed to about 8 hr of direct sunlight at temperatures not over 38° C. The concentration of the chemical in all the experiments was reduced from the original 10 ppm to 0 or 1 ppm after 8 hr exposure. It may be noteworthy that even a clear aqueous solution containing 10 ppm of sodium pentachlorophenate tested 1 ppm after the same period of exposure. The results were similar when the experiments were repeated. It was also found that following 8 hr of exposure to sunlight these preparations were only 0–20% effective against *Australorbis glabratus* within a 24-hr period.

Under field conditions mud and sunlight may be important factors in reducing the efficacy of some molluscacides. The effects of mud can be minimized by applying the chemicals when the waters are clear and by exercising care not to disturb the mud during the period of treatment. Proper allowance should be made when chemicals must be applied in muddy waters. Indications are that sunlight is a major factor in reducing the concentration of some chemicals in very shallow open waters but not in deep waters. In the field, sunlight appears to be less of a factor than mud in reducing the concentration of chemicals because most of the waters are shaded by rooted and floating vegetation and often by high banks.

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Nonfixation of Carbon Dioxide into Organic Acids in Blood[1]

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Although there is evidence in the literature for the existence of the physiologically important organic acids of the Krebs cycle in blood, data on their physiologic origin or role in this fluid are far from complete. Doubtless the lack of methods of isolation for these acids has contributed to the enigma. The extent to which tissue acids are diffusible into blood, and the scope of the function of the cycle in blood as compared to some other tissue such as liver, have not been considered. One approach to these problems was recognized when labeled organic acids were chromatographically isolated from tissues of mice injected in-

[1] This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, USPHS.

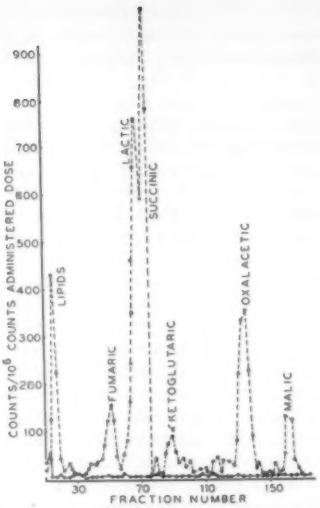

FIG. 1. Typical chromatograms for blood and liver extracts from a mouse sacrificed 5 min after a single injection of C^{14}-labeled bicarbonate. ● smooth line, 0.43 g whole blood; ○ dotted line, 1.0 g liver.

traperitoneally with labeled bicarbonate. Such acids containing the isotope were obviously synthesized by the animal, and the extent to which these labeled acids appeared in blood should be a function of their rate of synthesis by, or their diffusibility into, the blood from tissues elaborating them. In this report are presented data which indicate that organic acids labeled *in vivo* by mice injected with $NaHC^{14}O_3$ show concentrations in the blood less than 10% of those in the liver, and CO_2 fixation into organic acids by blood does not occur, or at least is not measurable.

In these studies 0.2 ml of 0.1 *M* $NaHC^{14}O_3$ containing 250 μc as isotopic carbon[2] were injected intraperitoneally into mice weighing approximately 2.0 g. The animals were sacrificed by decapitation 5–10 min following the injection. This time interval was selected because within it the incorporation of carbon into the acids of the tissues studied was maximal, *in the mouse*. Extracts (*1*) of the tissues were chromatographed on silica gel (*2*). Radioactive assay of the effluent, identification of the effluent organic acid, and other experimental details are reported elsewhere (*3*). A chromatogram representing a typical experiment is shown in Fig. 1.

The results (Table 1) indicate that the total activity of the organic acid extracts of whole blood was not greater than 8% of that of the liver extracts. From the percentage of activity shown by each of the several acids, no selective or preferential diffusion of any single organic acid from liver into blood can be adduced. When the blood in three experiments was assayed for labeled bicarbonate, these samples showed 1.8×10^4, 1.9×10^4, and 1.2×10^4 epm/g blood/10^6 counts administered dose. This would seem to indicate that, although $C^{14}O_2$ was available for fixation of the carbon into the organic acids, there was no such synthesis in the blood. A lack of mechanisms in the blood comparable to those in liver for the fixation of $C^{14}O_2$ into the organic acids could account for this failure of incorporation. The labeled bicarbonate in blood, however, was available to kidney and muscle tissue, both of which showed a greater incorporation per gram tissue than blood, but less than one fourth of that shown by liver. The protein residues from the organic acid extracts of the blood had no appreciable activity, thus ruling out the possibility that the acids synthesized in the liver, after diffusion into the blood, were bound to protein.

In view of what is known of the concentrations (*4*) of organic acids in blood and the above-reported total activities of the organic acids in blood and liver, it might be that those organic acids naturally occurring in blood diffuse largely from the liver. For example, fumaric acid in blood has a concentration of "less than" 0.5 mg% (*1, 4*), whereas in liver the concentra-

[2] The radioactive carbon was obtained as $BaC^{14}O_3$ from the Atomic Energy Commission, Oak Ridge, Tenn.

TABLE 1

COMPARISON OF ORGANIC ACID EXTRACTS FROM LIVER AND BLOOD OF MICE INJECTED INTRAPERITONEALLY WITH LABELED BICARBONATE

Tissue	Time (min)	Tissue (g)	Total extract activity/g tissue	Percentage of total extract*				
				Lipids	Fumaric	Succinic	Oxalacetic	Malic
Liver	10	1.2	11,256	37.5	5.4	5.8	14.0	—
	5	1.0	75,460	3.8	3.8	33.9	40.7	3.2
	5	0.7	78,654	12.9	5.1	29.1	9.2	9.2
	5	0.7	80,318	16.0	14.2	27.7	3.6	3.6
Whole blood	10	0.58	915	5.0	15.0	23.4	19.9	5.0
	5	0.79	645	15.6	15.0	17.4	0.7	0.01
	5	0.57	3,800	10.2	17.2	21.8	2.4	4.2
	5	0.76	5,160	10.0	15.0	25.0	4.6	6.6

* No discrete chromatographic peaks were obtained from blood (Fig. 1). Values shown for blood in the table were obtained by adding the observed radioactivity within each chromatographic zone described by effluent organic acids from liver on the chromatogram.

tion is about 6 mg%, and this ratio of 1 to some value greater than 10 is also reflected in the total activities shown above.

Since the rate of diffusion of these acids into blood seems to be slow, and since mechanisms for fixing carbon dioxide into organic acids in blood appear to be lacking, studies involving carbon dioxide fixation for the time intervals used above can be carried out *in vivo*, and yet each organ will synthesize its carbon-labeled organic acids appreciably uncontaminated by acids formed at another site in the same animal.

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Decreased Activity and Energy Balance in the Hereditary Obesity-Diabetes Syndrome of Mice[1, 2]

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The hereditary obesity-diabetes syndrome, previously described (*1, 2*), is a recessive Mendelian entity characterized by an adult weight up to three or four times the normal, sterility (*3*), atrophy and ulcers of the skin, and decreased life span. Histopathological studies (*4*) reveal considerably enlarged islets of Langerhans, with no other morphological evidence of endocrine disturbance. Total basal oxygen consumption is low (*5*), with basal metabolic rates 40–50% below normal. Radioiodine uptake is not decreased (*6*). Fasting respiratory quotients are normal, nonfasting respiratory quotients are high (*7*). The caloric intake of the obese mice (*1*) is about 25% higher than that of the nonobese. If the mice are allowed to select nutrients freely, the obese mice choose a higher proportion of fat and a lower proportion of carbohydrate than the nonobese. The animals become diabetic at about the tenth week of life (*2, 7*). The diabetes is characterized by extreme insulin resistance and sensitivity to the amount and the nature of the diet. The obese animals show a decreased ability to oxidize acetate fragments (*8*); these are deposited instead as fatty acids. The hyperglycemia appears to be due to a block of the hexokinase reactions secondary to this primary genetic block and induced by pituitary diabetogenic (growth) hormone (*7, 9*). This secondary block has been implicated in the etiology of the hyperphagia in the light of the glucostatic scheme of regulation of food intake (*10*).

Obese animals are visibly less active than nonobese litter mates. It was the purpose of the study reported here to quantitate this difference in activity between obese and nonobese animals, and to see how it varied with age and degree of obesity. The contribution of this decrease in expenditure for work to the imbalance between energy intake and output could then be evaluated.

Thirty-six mice, 12 nonobese animals 4 months old, 12 obese litter mates, and 12 young (2 months) obese animals of the same weight as the nonobese were placed in activity (squirrel-type) cages equipped with wheels 36 cm in diameter rotating freely enough to prevent any climbing and to insure that all animals sat at the bottom of the wheel under comparable conditions. A counter registered the number of revolutions. The animals were fed Purina chow pellets and were allowed to drink water *ad lib.* The experiment lasted 21 days, with the number of revolutions recorded at 9:00 A.M. and 5:00 P.M. The rooms in which the animals were kept were maintained at constant temperature (24° C) and were illuminated from 9:00 A.M. to 5:30 P.M. Table I gives the starting weights, rates of weight change during the experimental period, average daily activity, and average daytime and nighttime activity rate of the obese, young obese, and nonobese animals.

TABLE 1*

	Obese (4 mo old)	Young obese (2 mo old)	Nonobese (4 mo old)
Starting wt (g)	51.2 ± 2.5	27.8 ± 3.0	26.9 ± 2.2
Wt variation (g/week)	+ 1.8 ± 0.9	+ 3.6 ± 1.4	− 1.2 ± 1.0
Total daily activity (rev/day)	74 ± 40	355 ± 233	4783 ± 1253
Daytime activity rate (rev/hr)	4 ± 2	14 ± 4	102 ± 5
Nighttime activity rate (rev/hr)	3 ± 2	13 ± 2	240 ± 32

* Starting weights, rates of weight change during experimental period, average daily activity and diurnal activity rhythm of obese, young obese, and nonobese mice. The values given are average (mean) values. The figures following ± are standard deviations.

It is immediately apparent that the difference in spontaneous activity between obese and nonobese animals is enormous. In fact, obese animals are practically inactive. This inactivity is not solely the result of extreme obesity but, in fact, precedes it, as is shown by the comparison of activity rates of nonobese animals and of young obese mice of the same weight. Incidental to this difference in average daily activity, the difference in activity rates during night (darkness) and day (illumination) conditions, very marked in nonobese animals, disappears in the obese. Although

[1] This work was supported in part by grants-in-aid from the National Institute of Arthritis and Metabolism, National Institutes of Health, USPHS, Bethesda, Md.; Nutrition Foundation, Inc., New York; and the J. M. Kaplan Fund, Inc., New York.

[2] As in previous studies, the mice used in these experiments were obtained through the kindness of Margaret M. Dickie, of the Jackson Memorial Laboratory, Bar Harbor, Me.

nonobese animals, given the opportunity to exercise by being transferred to activity cages, lose some weight during the first 2 weeks (weight then stabilizes and activity rates decrease slightly), no such reaction is demonstrated by the young or the older obese animals. In much older animals not included in the main experiment (age over 8 months, weight over 60 g) the number of revolutions/day dropped to less than 2 or 3.

The fact that decrease in activity precedes marked obesity makes it possible to ascribe to this decrease in activity a role in the etiology of the obesity. The weight differences between obese and nonobese animals have been found to be accounted for almost exclusively by fat (*11*). Weight increases of 15–20 g/month in adult obese mice are frequently observed. The young obese mice in the experiment reported here, for example, were accumulating fat at the rate of 16 g/month. It is therefore readily seen that differences of food consumption between obese and nonobese animals of the order of 25% (*1*) can account for the development of the obesity only if the extra 5 calories/day consumed by the obese are converted into body fat with a net efficiency of about 100% instead of one of the order of 25%, as previously postulated. In some cases the increase in food intake over the nonobese level cannot *per se* account for the obesity. The explanation for this fact, as well as for the improbable efficiency level, lies in two findings: (*a*) The resting metabolism stays the same when the body weight increases by 200 or 300% (*5*); in fact, the total oxygen consumption per animal is somewhat lower in obese than in nonobese animals. (*b*) Far less energy is used in movement by the obese than by the nonobese animals, and the cost of moving the body weight does not increase as obesity develops because activity is almost nil. It can be calculated from respiratory data (*5*) that nonobese animals require 11 cal/day for basal expenditure. If specific dynamic action is taken as 10% of the total intake of 20 cal, it is readily seen that 7 cal are left for spontaneous activity and some fat formation. The same calculations applied to obese animals give 9.5 cal for basal expenditure, 2.5 for specific dynamic action, and 13 cal for fat formation and exercise, with the latter a negligible item. Decrease in activity therefore represents a not unimportant factor in the etiology of this form of obesity.

Two other observations are relevant to the problem of the relation of exercise to the development of obesity in these mice. First, when obese mice carry the waltzing gene and are in constant rotary movement in their cages, their weight rarely exceeds 40 g instead of twice that value. Second, it has been shown previously (*7*) that when obese mice are pair-fed with nonobese litter mates, their weight stabilizes at the level reached before paired feeding was started, neither increasing nor decreasing. As the resting over-all metabolism of obese animals is not greater than that of nonobese, they should, if their expenditure for work remained lower than that of the nonobese, still gain weight under paired feeding conditions. Actually, only a few mice do. The explanation of this apparent paradox lies in the fact that total or partial fasting increases the activity of obese mice proportionally much more than that of the nonobese. Total deprivation of food increases the number of revolutions per day by 50–60% for the nonobese—it brings it up to normal nonfasted levels (4000–5000) for young obese animals. Paired feeding, which represents a curtailment of intake of about 25% for the obese, is found to bring about a rate of activity of 1000–2000 revolutions per day. When the heavier weight of the obese animals is taken into account, the increase in work expenditure added to the decrease in calorie intake is seen to be sufficient to account for the cessation of weight increase.[3]

The relation of the decreased activity of the obese animals to their decreased resistance to cold is discussed in another publication (*12*), as is the relation of activity to human obesity (*13*).

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[3] In private conversation with Thomas H. Maren, of the American Cyanamid Co., it was found that he had independently arrived at the conclusion (unpublished) that part of the excess fat of the obese animals must be derived from energy devoted to exercise in the nonobese animals.

Mast Cells and Susceptibility to Experimental Atherosclerosis[1]

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It has been known for the past four decades that lipemia and atherosclerosis can be produced easily by cholesterol feeding in the rabbit, whereas the rat is a notoriously refractory species (*1*). The reason for the remarkable resistance of the latter species is unknown and has been the subject of considerable speculation. It has been attributed in turn to a very efficient vasa vasorum system, to a very low resting blood cholesterol

[1] This investigation was supported by the Banting Research Foundation and the National Research Council of Canada.

[2] The author is indebted to Margaret McLean and Jean Fairley for their valuable services in preparing numerous histological slides.

level, and to an unusually rapid clearance of intravenously injected cholesterol (*1*).

In recent years, heparin has been shown to prevent lipemia following fat meals (*2*) and to "wipe out" the giant lipoprotein molecules that appear in the blood of atherosclerotic patients and cholesterol-fed rabbits (*3*). Furthermore, in agreement with the claim of Graham *et al.* (*4*), we have presented evidence that heparin will retard the development of atherosclerosis in cholesterol oil-fed rabbits (*5, 6*).

In view of these data, and since it is highly probable that heparin is produced by the mast cells in the connective tissue (*7, 8*), we compared the histological mast cell content of numerous organs from the rat and the rabbit.

The following materials were examined in each of 4 Wistar albino rats (3 males and 1 female): skin, skeletal muscle, heart, brain, aorta, thymus, lung, liver, spleen, kidney, pancreas, jejunum, mesentery, and omentum. The same materials and, in addition, the adrenal, the gonad, and the uterus or epididymis were examined in each of 5 white rabbits (3 females and 2 males).

All organs were fixed in a mixture of 16 parts 95% alcohol, 2 parts 40% formaldehyde, and 1 part glacial acetic acid. In all instances, random sections from the whole organ were stained as follows: (1) aqueous 0.5% toluidine blue, slightly alkaline; (2) aqueous 0.5% thionine blue, slightly alkaline; (3) aqueous 0.5% toluidine blue, buffered at pH 4.5–4.7 (*9*); (4) alcoholic 0.5% thionine blue (in 70% alcohol) with no solution of less than 70% alcohol concentration used between deparaffinization and mounting (von Möllendorf's all-alcoholic procedure [*10*]).

The tissues of the two species were stained simultaneously, in the same solutions. Mast cells were identified on the basis of their metachromatic granules. Their concentration in tissues was graded on a semiquantitative scale.

The results obtained by all staining methods were essentially identical and can be summarized as follows:

With the exception of the brain and the spleen—which contained no mast cells—the connective tissue in all other organs of the rat was constantly supplied with mast cells. These cells were extremely abundant in the thymus and the integument, numerous in the circulatory, respiratory, and urinary systems, and scarce in the digestive system.

By contrast, with the exception of the skin, the skeletal muscle, the heart, and the intestine—where very few cells with metachromatic granules were seen—we could find no mast cells in the other organs of the rabbit.

Recently, Bensley (*11*) introduced a new dye, alcoholic pinacyanol erythrosinate, which is a differential tissue stain and, in addition, selectively stains mast cells. Examination of 16 formalin-alcohol–fixed organs from each of two additional rats and rabbits with this excellent stain substantiated the results obtained by the previous methods.

In view of these findings, it appears possible that the great atherosclerosis susceptibility of the rabbit may be due to the rudimentary development of the heparin-producing gland in this species, and that the immunity of the rat may be caused by its much greater capacity for heparin secretion.

Records of species differences with regard to mast cells are contained in the earliest histological literature (*7, 10, 12*), although no systematic comparison of the rat and the rabbit has been made to date. Since no special significance could be attached to these findings in the past, and since the general trend has been to establish the mast cells as a constant component of vertebrate connective tissue, such contested reports as were made concerning the rabbit remained in the background. Thus, shortly after Ehrlich's (*13*) identification of the mast cells with metachromatic stains, his pupil Westphal (*14*) reported that mast cells occur abundantly in rats, bats, dogs, goats, and bovines but only sparsely in rabbits, birds, and cats. Shortly afterward, Raudnitz (*15*) reported that he could not find any mast cells in rabbits. Schreiber and Neumann (*16*), however, claimed that mast cells abound in some rabbit strains but are sparsely present in others. Also, von Möllendorf (*10*) and Michels (*12*) pointed out that rabbit mast cells are very difficult to demonstrate after aqueous fixatives and aqueous staining solutions.

It may be relevant to note that the rabbits employed in the present study have been verified to be highly atherosclerosis susceptible. Daily feeding of 1 g cholesterol (dissolved in 14 ml Mazola) produces macroscopic lesions after 5 weeks in this strain. Conversely, the rat strain studied proved refractory to comparable treatments.

The possibility that atherosclerotic or senile human subjects may present a mast cell deficiency similar to that of atherosclerosis susceptible rabbits is being investigated in this laboratory.

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Comments and Communications

Snares Awaiting the American Scientist

THE following contentions are highly political, and at least one of them is patently false:

> Present American foreign policy uses diplomacy as a weapon for the aggravation of hatreds, and not as a means of agreement.
>
> There are two varieties of freedom. Americans have political freedom for which they are willing to fight. Such a fight is futile, since this kind of freedom is of no concern to the vast majority of the world's people, for they have never had it. The kind of freedom for which these people fight is freedom from hunger, want, and disease.
>
> There is one policy left which can save us: an active, positive policy for peace; but, unfortunately, this country has prematurely closed discussion on this policy.

These contentions appear in Melba Phillips' article bearing the title "Dangers Confronting American Science" in the October 24, 1952, issue of SCIENCE (*1*). The publication of this article, of itself, constitutes an obvious refutation of the contention that this country has closed discussion on an active, positive policy for peace, for this very policy is agitated in the article.

To anyone who has followed the discussions on the world crisis in the usual media in which they are given currency, such as the newspapers, political periodicals, and radio programs, the views of Dr. Phillips are not new. They have been set forth on many occasions, in many forms, and in other countries. Their appearance, however, in the pages of a journal devoted to science constitutes a novelty which is sure to attract for them more attention than they usually receive, by now, when placed on exhibition in their natural habitat.

Presumably on the theory that the sanctity of science is the chief concern of the American scientist, Dr. Phillips confronts him with her list of dangers to science which she says result from our foreign policy. She evidently feels that this is the effective way to startle him into helping to destroy that policy. Typical of her approach is her charge of the perversion in this country of the classical goals of science. This perversion, she says, results from the use of the great bulk of our scientific budget for the creation of weapons of destruction. In order to establish this perversion she sets up the premise that one of the classical goals of science is the discovery of nature's secrets for humanitarian purposes. This is a glittering premise, but it does not glitter with the hard gem of fact, for it is well known that Galileo (if "classically" means anything it must refer to the science of the 17th and 18th centuries) had a lively interest in the technical problems of war and required no prodding from his Medici patrons to lend his talents to such nonhumanitarian concerns as ballistics, stability of firearms, and strength of fortifications. It is well known that he used to frequent the great arsenal in Venice. In the "First Day" of the "Dialogues" (*2*) he actually praises the arsenal as a stimulus to thought; and the "Fourth Day" is devoted to a discussion of "Projectiles." And, of course, it would have been difficult to persuade a combatant who had just suffered a direct hit from a piece of improved Florentine artillery, providing he was still in condition to argue the matter, that Galileo's discovery of the parabolic nature of the trajectory of a projectile was inspired by humanitarian goals.

Thus, it seems to me that any "perversion" which confronts us here is only that present in Dr. Phillips' definition of the classical goals of science. Bertrand Russell with his usual insight defines science in terms of its functions. He says simply that science has two functions: one, to enable us to know things; and two, to enable us to do things (*3*). In the light of this definition it is clear that American science of today is no different from the classical science of Galileo and all the others.

There are many other things to say about Dr. Phillips' portrait of American science, but pausing only long enough to note its execution in a style heavily charged with militant emotion, its immoderate emphasis here, its adroit understatement there, all overlaid with a translucent pall of bias which makes it difficult to establish the faithfulness of the portrait to its subject, we pass on to the consideration of her "political context," which is the crux of the article. As a way out of the intolerable danger of losing his scientific freedom and all the other dangers which confront him, the American scientist is exhorted by Dr. Phillips to look to his political power. Leading up to this exhortation, there is first a statement to the effect that in this country only two alternatives are being considered as possible outcomes of the world crisis: (1) world victory by the Soviet Union; and (2) an all-out effort by us, even total war. Then, despite her announced intention to discuss both of these alternatives, she curiously enough neglects alternative (1), and confines her analysis to alternative (2), pointing out that the only two possible eventualities here would be the indefinite prolongation of present tension or total war, in both of which cases civilization and science would be the chief casualties. It is interesting to note that at the end of her analysis of alternative (2) there occurs the following observation: "If these were the only alternatives, then for one who believes Communism to be an ultimate and unmitigable evil there would be little hope indeed." I suppose this implies that there *is* hope for one who does *not* believe Communism to be an ultimate and unmitigable evil.

However this may be, Dr. Phillips then announces the discovery of another alternative which surpasses either (1) or (2). This alternative is *Peace*. But, recognizing that *Peace* is not enough (she notes acutely

that everyone is in favor of *Peace*), she then gets around the difficulty by specifying that there must be an "active, positive policy for peace." She hints that she has a blueprint for such a policy, but does not offer it "at this point." Nor is it explained why she withholds it at this time of crisis. But she does recommend as a "positive alternative to present American foreign policy" a pamphlet entitled *"Steps to Peace—A Quaker View of U. S. Foreign Policy."* In her conclusion she offers what seems to be one item of her blueprint, viz., the necessity on our part of extending aid in the development of backward countries in order to gain their goodwill. It is to be hoped that the rest of her blueprint constitutes an original contribution. The item she discloses does not. It is set forth and fully developed in this pamphlet "Steps to Peace."

"Steps to Peace" is a 64-page pamphlet dated April 1951, prepared for the American Friends Service Committee by a 15-man committee. There can be no question of the deepest devotion of these men, as Quakers, to the cause of humanity. They have addressed themselves to the task of analyzing the causes of what they term the failure of American Foreign Policy, and of presenting their alternative thereto. As to their fitness for this job they point to their "knowledge of the hearts and minds of people the world over." The cogency of their analysis of the world crisis may be judged from the following examples of it. They say that "our insecurity stems from the rapid expansion of Russian influence, but we should recognize that a major reason for this expansion is the economic appeal of Communism." At this point the reader thinks of Czechoslovakia and wonders whether the committee did when they wrote that. Another example is the statement of the general American belief that the Russian Communist system has suppressed the freedom of speech, thought, and political action of its citizens, that the secret police power and forced labor exceeds anything known in Czarist times, etc. They then comment: "It is entirely possible that opportunities for first hand study of Soviet life and for normal contacts with the various peoples of the Soviet Union might reveal serious gaps or distortions in this widespread American conception of Soviet conditions. Until such opportunities are granted, however, it is natural for Americans to look on the claim of Soviet apologists with healthy skepticism." Healthy skepticism, indeed! Apparently there is no assumption the committee is unwilling to entertain, no matter how unequivocal history may be concerning its implausibility. The pattern revealed in this quotation (and others could be cited) may be described as first agreeing to entertain a wildly improbable supposition as true; then, sensing a challenge to such view, seeming to accept the alternative possibility that there may be nothing to it, after all. The committee, like Polonius, discerns in yonder cloud the shape of a camel, but under the relentless Hamlet-prodding of their doubts, agrees that it may be instead a weasel, or even yet a whale.

However, the most conspicuous accomplishment of the committee is in writing a 64-page pamphlet packed with comments on the greatest variety of world problems and their causes, and including what is perhaps the most complete collection ever assembled under one cover of every charge ever leveled at U. S. foreign policy, without once pausing to consider whether, and how, the Communist ideological requirement for destruction of the democratic world has been fundamental in the framing of that policy. There is just one instance in the whole pamphlet where the committee reveals even its awareness of such a thing as Communist doctrine. The reference thereto is brief, and is used *not* to expose the doctrinal requisite for victory over the capitalist world, but to explain why, because of the "Marxist doctrine of capitalist attack, it is at least conceivable that defensive considerations are primary to Soviet plans with respect to the Red Army. To consider them in this light may be risky, but any policy involves risk . . ." (p. 29). The question is: "How conceivable?"

A long time ago there was a group in Troy which found it conceivable that the famous snare, the "Trojan Horse," was something other than it turned out to be. How little conceivable it is that Soviet plans for the Red Army are primarily defensive may be judged from the following conclusion by an expert on Soviet foreign policy: "An explanation of Soviet policy which dismisses the Revolution would seem to be an explanation which neither the facts nor Soviet writings warrant. The basic and inescapable relation of the Soviet State to other states is one of conflict. And for a full understanding of the Soviet attitude, it is necessary to realize that the conflict is one in which the outcome is a foreordained victory for the Soviet State and with it the international proletariat. To try to comprehend the Soviet outlook and to dismiss the inevitability of the world revolution is as idle as to comprehend the outlook of medieval man and to dismiss the reality of the Last Judgment" (*4*).

Concerning the committee's "Alternative Program," little need be said beyond a brief description of the first item thereof. This is the necessity, simply, of reaching agreement by negotiation. To the objection "Well, that is what we have been trying to do for a long time," their answer is we must negotiate harder, as hard as we can. They outline specific requirements for harder negotiation, and offer many practical hints such as 'If negotiators become discouraged or exhausted, they should be replaced" (p. 36).

Dr. Phillips hails "Steps to Peace" as a substitute for our present foreign policy. I do not share her enthusiasm. I feel, as do the vast majority of our people, that whereas our foreign policy may not carry us even within hailing distance of the fair millenium, and to that extent may be a poor thing indeed to contemplate, yet it is an unavoidable policy which has been pushed into our hands by an implacable foe, and, until he announces a change in his plans, we have to hang on to it for dear life. One thing that gives us comfort in this grim enterprise is the good company we

have with us, viz., Dean Acheson, Eleanor Roosevelt, and Adlai Stevenson, to name but very few; all, it should be noted, people of the very deepest humanity.

In 1950 Bertrand Russell said: "The human race could, here and now, begin a rapid approach to a vastly better world, given one simple condition: the removal of mutual distrust between East and West. I do not know what can be done to fulfill this condition. Most of the suggestions I have seen have struck me as silly. Meanwhile the only thing to do is to prevent an explosion somehow and to hope that time may bring better wisdom." (l.c., p. 64) Up to now no word has come that, since the appearance of the committee's pamphlet or Dr. Phillips' article, the British sage has modified these 1950 views.

JOSEPH K. MARCUS

27 W. 96th St., New York City

References

1. PHILLIPS, M. *Science*, **116**, 439 (1952).
2. CREW, H., and DE SALVIO, A. *Dialogues Concerning Two New Sciences, by Galileo.* New York: Macmillan (1914).
3. *Matchette Foundation Lecture* No. 3, p. 21.
4. BELOFF, M. *The Foreign Policy of Soviet Russia*, Vol. 2. Oxford: Oxford Univ. Press, 390, 392 (1949).

Stress Research

AN ever increasing number of articles deals with problems pertaining to research on "stress" and the so-called "adaptive hormones" (ACTH, STH, corticoids, adrenergic substances, etc.).

In 1950, the Institute of Experimental Medicine and Surgery of the University of Montreal initiated the publication of a series of reference volumes entitled *Annual Reports on Stress* (Acta Medical Publishers, Montreal), in which the entire current world literature is surveyed every year (usually between 2000 and 4000 publications). Up to now, we have had to compile the pertinent literature partly from medical periodicals, monographs, abstract journals, and partly from reprints sent to us by the authors themselves. Of all these, reprints proved to be the best source of data which we felt deserved prompt attention in our annual reports. Hence, in the past, we have sent our several thousand individual reprint requests to authors whom we knew to be currently engaged in research on stress and allied topics.

We would like to encourage investigators interested in stress research to send us their reprints for this purpose as soon as they become available.

HANS SELYE
ALEXANDER HORAVA

Institute of Experimental Medicine and Surgery
University of Montreal

"The Earth Is Born"

I RECENTLY sent a letter to *Life* protesting certain points in regard to its quite striking pictures and the text of "The Earth Is Born." *Life* edited my letter by removing my remarks relative to granite floating in its liquid, and I wish to present the full letter for publication in SCIENCE. In 1950, there was a conference at Rancho Santa Fe on the origin of the earth, attended by chemists, geologists, and astronomers. The geologists concluded rather definitely, I thought, that a non-liquid origin of the earth was probable, and convinced me of the reasonableness of their arguments (*1*). I suppose that all these men dashed off letters to *Life* relative to certain details of its story and fared even more badly than I did, since their letters evidently were not published at all. My letter follows:

"I wish to compliment *Life* on the magnificent pictures of "The Earth Is Born," but also wish to criticize these pictures in certain details on the basis of scientific fact and deduction.

"(1) Water is the only common substance whose solid, ice, floats on its liquid. The rocky materials of the earth sink in their molten liquids and therefore it is difficult to see how the continents were formed as great blocks of solid granitic masses floating in liquid or coming to rest on sunken platforms of basalt. I know of no statements of scientific workers recorded in the serious scientific literature that agree with this view. Moreover, when a mixture of silicates freezes the more dense constituents crystallize first and sink. If the earth was formed in a molten condition—and there is disagreement among scientific students on this point—then the continents were formed from the last liquid to become solid. On the basis of your story, God must have stuck close to this insignificant planet and given a helping hand at crucial moments. I prefer to believe that His laws of nature, including the differences in densities of solid and liquid rocky materials, were sufficient to accomplish the end result without further intervention. Unless this assumption is made, the whole course of the origin of the earth cannot be solved by scientists and belongs in the realm of folklore and mythology. Incidentally, the laws of floating bodies were discovered by Archimedes in the third century B.C.

"(2) If the moon was completed some 10,000 miles from the earth's surface, i.e., just outside the distance at which the tides would break it up, or 11,600 miles from the center of the earth, it certainly would have had an egg shape and as it subsequently moved away from the earth its shape must have changed to its present nearly spherical one. This would have caused a great break up of its surface, and the cracks in its surface should have some sort of concentric pattern about the center of the moon's face. I can see no such pattern. Moreover, the primordial egg-shaped moon would have a larger surface than the present spherical one and hence as the former changed to the latter, buckling of the surface should occur and folded mountains be formed. Fissures in the moon's surface are remarkably open and no folded mountains have ever been identified. Again, the earth contains large amounts of metallic iron and the moon does not. Would it not be well to give the cosmic chemical engineer some help in getting iron on the earth and little on the moon by keeping them some reasonable distance

apart? But what reasons are there for this short distance? Until I know the reasons, I simply do not believe it. Science does not consist of such dogmatic statements, but seeks to understand how and why things happen.

"(3) Lincoln Barnett says, 'Some theorists think that its substance was cold and wet, like snow.' This seems to refer to me, but if so, it is a complete misrepresentation of my ideas. I discussed a cold stage in the formation of the earth, but placed the temperature at which the earth accumulated at perhaps 1650° F.

"There are other points which I might criticize, but most of all it seems to me that *Life* should use in stories of this kind the results of scientific workers who have been willing to put their ideas and conclusions into serious scientific publications under their own names, so that they can be criticized by other scientists. Such ideas are more reliable in general than those which have not been so presented and criticized."

HAROLD C. UREY

Institute for Nuclear Studies
University of Chicago

Reference

1. SLICHTER, L. B. *Proc. Natl. Acad. Sci. U. S.*, **36**, 511 (1950).

Association Affairs

Gordon Research Conferences June 15–September 4, 1953

W. George Parks

University of Rhode Island, Kingston

THE Gordon Research Conferences, sponsored by the AAAS, for 1953, will be held from June 15 to September 4 at the Colby Junior College, New London, N. H., and the New Hampton School, New Hampton, N. H.

The conferences were established to stimulate research in universities, research foundations, and industrial laboratories. This purpose is achieved by an informal type of meeting consisting of scheduled lectures and discussion groups. Sufficient time is available to stimulate informal discussions among the members of the conferences. Meetings are held in the morning and in the evening, Monday through Friday, with the exception of Friday evening. The afternoons are available for recreation, reading, resting, or participation in discussion groups as the individual desires. This type of meeting is a valuable means of disseminating information and ideas that otherwise would not be developed through the normal channels of publication and scientific meetings. In addition, scientists in related fields become acquainted, and valuable associations, which have resulted in collaboration and cooperative efforts between different laboratories, have thus been created.

It is hoped that each conference will extend the frontiers of science by fostering a free and informal exchange of ideas among persons actively interested in the subjects under discussion. The purpose of the program is not to review the known fields of chemistry, but primarily to bring experts up to date as to the latest developments, analyze the significance of these developments, and to provoke suggestions as to the underlying theories and profitable methods of approach for making new progress. In order to protect individual rights and to promote discussion, it is an established requirement of each conference that all information presented is not to be used without specific authorization of the individual making the contribution, whether in formal presentation or in discussion. Scientific publications are not prepared as emanating from the conferences.

REGISTRATION AND RESERVATIONS

Each applicant must state the institution or company with which he is associated and the type of work in which he is most interested. Attendance at each conference is limited to 100.

The director will submit the names of those requesting attendance to the Conference Committee for each conference. This committee will review the names and select the members in an effort to distribute the requests as widely as possible among the various institutions and laboratories represented. The names selected will be returned by the Conference Committee to the director, who will notify those accepted as soon as possible. A registration card will be mailed with the notice of selection. Advance registration by mail for each conference is required. On receipt of the completed registration card and a deposit of $25.00 made payable to the Gordon Research Conferences, AAAS, registration will be completed. The deposit of $25.00 will cover the registration fee of $15.00 (except for academic individuals and students on personal expense who may apply for a reduction of $5.00), and the balance will be credited against subsistence expenses at the conference. The room rates are as follows: $2.50 per night per person in a double room with single beds; $3.00 per night per person in a single room; $3.50 per night per person in a single or double room with private bath (the number of rooms available with bath is limited; assignments are made in the order that applications are received). Meals served in the dining room are at the rate of $6.50 per day per person. Gratuities are provided for by an

additional charge of ten per cent, which is added to each bill. Members attending a conference are expected to live at the conference. If special circumstances warrant living elsewhere, a special registration fee of $25.00 is charged. This special fee has been established by the Management Committee so that all individuals will assume their proper share of the expenses of the conference. The daily service charge used in previous years has been discontinued.

A special fund is put at the disposal of the chairman of each conference by the Management Committee to assist scientists from academic and government institutions who cannot attend or participate because of financial limitations. This fund is provided with the object of increasing the participation of research workers of academic and government laboratories; it is limited to scientists and graduate students who have been invited by the chairman to attend a conference in order to present a paper, or because it is expected that they will make significant contributions during their stay at the conference.

It is the responsibility of each chairman and the director of the conferences to use this fund effectively in meeting the individual needs of the academic and government participants. It may be used to contribute toward traveling expenses and/or subsistence expenses. The money is to be used as an assistance fund only. Total travel and subsistence expenses normally will not be available.

A limited number of special grants is available in the amount of $200.00 each, or as much of this amount as is required, to assist qualified graduate students and postdoctoral fellows to attend a Gordon Research Conference. The selection of these students and fellows will be based on the recommendations of their professors, by a committee consisting of the chairman of the conference to be attended, the chairman of the Management Committee and the director of the conferences.

If it is necessary to cancel a reservation, the notice must be received in the office of the director three weeks prior to the conference. If such notice is received three weeks in advance of the conference, $20.00 will be refunded from the $25.00 deposit. No refund will be made for cancellations received within the three-week period.

The first meeting of each conference is held Monday at 9:00 A.M. EDST. The morning sessions, through Friday, are scheduled from 9:00 A.M. to 12:00 noon. The second session of each day is held in the evening from 7:30 to 10:00 P.M., Monday through Thursday. There are no Friday evening meetings. Conference members are expected to release their rooms not later than Sunday morning unless they have made a reservation for the next conference.

Public lectures, sponsored jointly by the college and the Gordon Research Conferences, will be given on Sunday evenings preceding the several conferences. Conference members usually arrive on the Sunday afternoon preceding the conference because it is not possible to obtain public transportation Monday morning in time to arrive for the opening meeting. The schedule of these lectures has not been completed.

Accommodations are available for a limited number of women to attend each conference, also for wives who wish to accompany their husbands. All such requests should be made at the time of the request for attendance, because the limited accommodations will be assigned in the order that specific requests are received. Children under twelve years of age cannot be accommodated. Rooms are available at several inns and hotels in both New London and New Hampton, if reservations are made in advance. Information on these inns and hotels will be supplied by the director on request. No dogs or other animals will be permitted in the dormitories.

Requests for attendance at the conferences or for any additional information should be addressed to W. George Parks, Director, Department of Chemistry, University of Rhode Island, Kingston, R. I. From June 12 to September 4, 1953, mail should be addressed to Colby Junior College, New London, N. H.

Program at Colby Junior College

PETROLEUM

A. H. Batchelder, *Chairman*; W. J. Coppoc, *Vice Chairman*

June 15: Combustion Symposium: G. H. Denison, *Chairman*; B. M. Sturgis, "Reactions of Hydrocarbons in Engines"; W. F. Anzilotti, "The Combustion of Hydrogen as Related to Knock." C. L. Brown, *Chairman*; E. B. Rifkin, A. Ross, "Engine Combustion as It Is Influenced by Tetraethyllead"; E. C. Hughes, "Some Effects of V. I. Improvers on Engines."

June 16: L. H. Flett, *Chairman*; F. D. Rossini, B. J. Mair, "Composition of the Lubricating Oil Fraction of the Ponca, Okla., Petroleum of the API Research Project 6." E. C. Hughes, *Chairman*; M. J. O'Neal, "Application of High Molecular Weight Mass Spectrometry to Oil Constitution."

June 17: W. J. Coppoc, *Chairman*; S. S. Kurtz, Jr., C. C. Martin, "Composition of Viscous Fraction of Petroleum as Revealed by Physical Property Correlations and Hydrocarbon Type Analysis." R. G. Capell, *Chairman*; R. G. Capell, F. S. Charlton, W. S. McClenahan, G. G. Rumberger, "Composition and Properties of Petroleum Waxes."

June 18: D. R. Stevens, *Chairman*; R. W. Schiessler, "Correlation of Properties of Pure High Molecular Weight Hydrocarbons." J. Turkevich, *Chairman*; H. Eyring, R. J. Moore, "Structure of the Liquid State and Viscosity of Hydrocarbons."

June 19: L. L. Withrow, *Chairman*; E. C. Knowles, F. C. Toettcher, R. E. Berry, "Stability of Lubricating Oil Fractions"; H. C. Brown, "Friedel-Crafts Catalysts and Complexes—An Interpretation of Friedel-Crafts Alkylation Reactions."

CATALYSIS

P. W. Selwood, *Chairman*; G. A. Mills, *Vice Chairman*

June 22: Ahlborn Wheeler, "Diffusional Processes in Heterogeneous Catalysis"; R. H. Wilhelm, "Diffusion Measurements in Particulate Systems"; N. R. Amundson, "Mathematical Problems in Reactor Design."

June 23: J. W. Mitchell, "Semi-conductivity, Adsorption, and Catalysis"; P. B. Weisz, "Electronic Phenomena in Chemisorption and Catalysis."

June 24: L. R. Maxwell, "Electronic Magnetic Resonance and Its Application to Solid Solutions"; J. A. Becker, "Chemisorption of Oxygen and Hydrogen on Tungsten as Observed in the Field Emission Electron Microscope."

June 25: A. T. Gwathmey, "The Influence of Small Amounts of Foreign Atoms on the Catalytic Properties of Metallic Single Crystals"; H. E. Farnsworth, "Measurements of Gas Adsorption on Single Crystals Using the Method of Low Speed Electron Diffraction"; Rufus Lumry, "Biological Catalysis."

June 26: Milton Orchin and Irving Wender, "The Role of Cobalt Carbonyls in Homogeneous Catalysis."

Separation and Purification

Charles B. Willingham, *Chairman*; A. Letcher Jones, *Vice Chairman*

June 29: George V. Downing, "Theoretical and Methodological Criteria of Chemical Purity"; Kenneth C. D. Hickman, "Mechanism of Evaporation of Liquids."

June 30: A. Letcher Jones, "Thermal Diffusion Separation of Organic Liquid Mixtures"; Carl S. Carlson, "Extractive and Azeotropic Distillation—Newer Developments and Unsolved Problems in These Fields."

July 1: Clyde Berg, "Hypersorption—Newest Unit Operation for the Separation of Gases"; Henry A. Kunkel, "Zone Electrophoresis"; Alsoph H. Corwin, "Separation and Purification of Minute Quantities of Material."

July 2: Robert S. Tipson, "Purification by Recrystallization"; Augustus R. Glasgow, Jr., "Purification by Crystallization and Fractional Remelting"; Robert V. Kleinschmitt, "Demineralization of Sea Water."

July 3: Daniel Swern, "Inclusion Complexes—Preparation, Properties, and Uses."

Polymers

Arthur V. Tobolsky, *Chairman*; W. H. Stockmayer, *Vice Chairman*

July 6: H. Mark, "Inorganic Polymers"; F. R. Eirich, "Polyvinyl Pyrrolidone"; F. S. Dainton, "Reversal of Polymerization."

July 7: G. W. King, "Configuration of Polymer Chains"; W. Kauzmann, "Configurational Changes During Protein Denaturation"; P. D. Bartlett, "Inhibitors, Retarders and Chain Transfer Agents in Vinyl Polymerization."

July 8: W. M. Thomas and J. J. Pellon, "Mechanism of Acrylonitrile Polymerization"; R. S. Boyer, "Internal Brownian Motion of Polymer Chains"; G. P. Schmitt, "Continuous Processes and Phenol Formaldehyde Resinification."

July 9: F. O. Schmitt, J. Gross, and J. H. Highberger, "Collagen"; L. Mandelkern, "Rates of Crystallization"; C. G. Overberger, "Some Aspects of Ionic Polymerization."

July 10: M. J. Roedel, F. W. Billmeyer, and C. A. Sperati, "Branching in Polythene."

Textiles

George S. Buck, *Chairman*

July 13: John A. Howsmon, "The Evaluation of the Submicroscopic Structure of Fibers"; Leon Segal, "Decrystallization of Cotton Cellulose."

July 14: R. J. Andres, "Pressure Dyeing of Man-Made Fibers"; Subject and speaker to be announced.

July 15: Pauline Beery Mack, "Recent Developments in the Science of Textile Maintenance"; Herman Bogaty, "Chemical, Physical, and Physiological Characteristics of Blended Fabrics."

July 16: Myron J. Coplon, "Influence of Temperature on Certain Tensile Properties of Various Textile Fibers"; Speaker to be announced, "Chemistry of Polymerization of Acrylics."

July 17: D. J. Montgomery, "Generation and Conduction of Electricity in Fibrous Materials."

Corrosion

H. P. Godard, *Chairman*; A. Wachter, *Vice Chairman*

A Critical Review of Modern Fundamental Concepts in Corrosion

July 20: Thermodynamics in Corrosion. Electrochemical Theory of Corrosion.

July 21: Chemical Kinetics in Corrosion. High Temperature Oxidation.

July 22: Reaction Mechanisms: Intergranular Corrosion, Stress Corrosion, Pitting Corrosion, Fretting Corrosion.

July 23: Reaction Mechanisms: Corrosion Fatigue Thermogalvanic Corrosion. Corrosion in Fused Salts and Molten Metals.

July 24: Corrosion in Non-Electrolytes.

Instrumentation

W. A. Wildhack, *Chairman*; R. H. Munch, *Vice Chairman*

July 27–31: James G. Baker, "The Operational Difficulties of Large Telescopes, and Future Trends Toward Giant Telescopes." Albert F. Sperry, *Chairman*; Panel Discussion: The Automatic Plant. John Trimmer, "The Basis for a Science of Instrumentology"; Harold W. Crouch, "Recent Advances in Photography and Their Applications in Science and Instrumentation"; Dudley Williams, "Nuclear Resonance Spectroscopy"; Marcus O'Day, "Remote Geophysical Measurements of the Upper Atmosphere"; Edward B. Cooper, "New Materials of Interest to Instrument Designers"; Reverend Daniel Linehan, S.J., "Recent Advances in Geophysical Instrumentation."

Elastomers

Maurice Morton, *Chairman*; John Rehner, Jr., *Vice Chairman*

August 3: Silicone Rubber and Its Reinforcement: E. G. Rochow, "Valence Structure of Organosilicon Polymers"; F. M. Lewis, "Nature and Properties of Silicone High Polymers"; E. L. Warrick, "Filler Phenomena in Silicone Rubber."

August 4: Mechanism of Reinforcement: A. M. Bueche, "Reinforcement of Silicone Elastomers"; B. L. Stearns, "Carbon Black Surface Activity and Reinforcement." Free Radicals: M. Szwarc, "Effect of Chemical Constitution on Bond Dissociation Energy."

August 5: Free Radicals: R. Simha, "Kinetics of Free Radical Depolymerizaiton"; J. Crabtree, "Cracking of Rubber by Free Radicals." Oxidative Degradation: S.

Baxter, "Mechanism of Oxidative Degradation of Rubber."

August 6: Oxidative Degradation: J. E. Field, "Infrared Study of Oxidation of Polymers"; J. O. Harris, "Ozone Protective Agents." Mechanical Degradation: R. Schallamach, "Abrasion Studies on Rubber"; R. Schallamach, "Tearing of Rubber."

August 7: M. A. Smook, "'Hypalon' S-2 Chlorosulfonated Polyethylene."

Food and Nutrition

B. F. Chow, *Chairman*; H. W. Howard, *Vice Chairman*

August 10: Anthony A. Albenese, *Chairman*; Biological Utilization of Isomers: Daniel Melnick, "Fatty Acids"; Robert C. Hockett, "Carbohydrates"; Anthony A. Albanese, "Amino Acids"; Federico Gomez, "Nutritional Problems in Mexico." H. J. Deuel, Jr., *Chairman*; Essential Fatty Acids: H. J. Deuel, Jr., "The Relative Biopotency of Different Essential Fatty Acids"; Ralph T. Holman, "Chemistry and Metabolism of Essential Fatty Acids"; Raymond Reiser, "The Intermediary Metabolism of Polyunsaturated Fatty Acids"; Arild E. Hansen, "Essential Fatty Acids in Relation to the Condition of the Skin."

August 11: W. D. McElroy, *Chairman*; Trace Elements in Nutrition: W. D. McElroy, General Introductory Remarks; C. L. Comar, "The Role and Requirement of Trace Elements in Animal Nutrition"; D. J. D. Nicholas, "Soil-Plant Relationships in Trace Element Nutrition"; Alvin Nason, "The Catalytic Function of Trace Elements in Enzyme Systems of Plants and Animals." Harry Spector, *Chairman*; Emergency Feeding; Military Survival Feeding: David Schwimmer, "Protein Metabolism at Low Caloric and Water Intakes"; Austin F. Henschel, "Climatic Factors in Survival Physiology." Civilian Disaster Feeding: John J. Hurley, "National Civil Defense Program"; Herbert Pollack, "Regional: City and State Program."

August 12: Charles Rosenblum, *Chairman*; Tracer Techniques in the Food and Pharmaceutical Industries: Charles Rosenblum, Introductory Remarks; Anthony J. Glazko, "Pharmaceutical Applications of Isotopes"; F. E. Kelsey, "Pharmacological Testing with Isotopically Labeled Drugs"; R. R. Baldwin, "Isotope Tracers in Food Processing"; R. S. Harris, "Use of Isotopes in Nutritional Biochemistry Research."

August 13: Robert S. Goodhart, *Chairman*; Vitamin B_{12}: F. H. Bethell, "The Absorption of Vitamin B_{12} and the Nature of the Intrinsic Factor"; R. Engel, "The Relation of Vitamin B_{12} to Methylating Substances with Comments on Vitamin B_{12} and Hepatic Disturbances"; J. Meites, "Some Comments on Vitamin B_{12} and Endocrine Function"; R. W. Vilter, "Some Metabolic Roles of Vitamin B_{12} with Emphasis on Factors Affecting Utilization"; C. C. Ungley, "Clinical Investigations on Crystalline Vitamin B_{12}"; Robert Funaro, "Observations on Vitamin B_{12} as a Growth Factor in Children on Diets Low in Animal Protein"; W. F. Alexander, "Vitamin B_{12} and the Metabolism of Nerve Tissue"; J. R. Couch, "Vitamin B_{12} Deficiency and Congenital Abnormalities."

August 14: H. W. Howard, *Chairman*; Food Sterilization: Samuel A. Goldblith and Bernard E. Proctor, "The Mode of Action of Sterilization by Heat, Chemical and Physical Means"; Lloyd A. Hall, "Epoxide Sterilization for Commercial Use"; Charles R. Phillips and Saul Kaye, "Chemical Sterilization of Rations."

Medicinal Chemistry

Jackson P. English, *Chairman*; K. J. Brunings, *Vice Chairman*

August 17: Virus Diseases: Salvador E. Luria "Virus Production as a Cytochemical Problem"; J. L. Melnick, "*In Vitro* Cultivation of Animal Viruses." Anemia and Vitamin B_{12}: Karl Folkers, "Chemistry and Structure of Vitamin B_{12}"; C. C. Ungley, "Chemotherapeutic Action of Vitamin B_{12}."

August 18: Drug Action: Bernard Brodie, "Factors Determining Drug Distribution." Mechanisms Involved in the Metabolism of Drugs: Sidney Udenfriend, "Hydroxylation Mechanisms"; Bert LaDu, "Dealkylation Mechanisms"; Julius Axelrod, "Species Differences in Drug Metabolism"; James Shannon, "The Study of Drugs in the Human Subject."

August 19: James A. Bain, "Biological Mechanisms of the Action of Drugs on Tissue Cells"; George H. Hitchings, "A Biochemical Approach to Chemotherapy." Anti-inflammatory Agents: Edward Lowman, "Introduction to Collagen Diseases"; Robert Domenjoz, "Pharmacological Evaluation of Anti-inflammatory Agents—Pharmacology of Butazolidine"; Edward Lowman, "Clinical Evaluation of Anti-inflammatory Agents."

August 20: Anticoagulants: Walter H. Seegers, "Chemistry of Blood Coagulation"; John J. Denton, "Chemistry and History of Anticoagulants"; Charles Brambel, "Pharmacological and Clinical Studies on Anticoagulants"; C. B. Anfinsen, "Anticoagulants in Arteriosclerosis."

August 21: Narcotics and Narcotic Antagonists: Karl Pfister, "Chemistry"; Charles Winter, "Pharmacology."

Vitamins and Metabolism

B. Connor Johnson, *Chairman*; Grace A. Goldsmith, *Vice Chairman*

August 24: H. E. Sauberlich, "Functions of the Citrovorum Factor"; Marian E. Swendseid, "Conversion of Folic Acid to a Citrovorum Factor by Hemopoietic Tissue"; Ulrich Weiss, "Intermediates in Aromatic Biosynthesis." Discussion, Charles Gilvarg: Nathan H. Sloane, "Studies on the Staphylococcus Growth Stimulatory Factors."

August 25: E. Lester Smith, "New Studies on Vitamin B_{12}"; C. C. Ungley and A. L. Latner, "Vitamin B_{12} and the Intrinsic Factor"; H. G. Wijmenga and N. V. Organon, "Investigations on Intrinsic Factor"; J. W. G. Porter, "New Forms of Vitamin B_{12}." Discussion, J. J. Pfiffner: J. W. G. Porter, "Function of Antibiotics in Growth Stimulation." Discussion, T. D. Luckey: Kenneth L. Blaxter, "The Role of Vitamin E in the Nutrition of the Calf." Discussion, J. K. Loosli.

August 26: Elaine P. Ralli, "Pantothenic Acid in Relation to Stress"; Mercedes Thérien, "Ascorbic Acid and Cold Weather Stress"; A. E. Axelrod, "Role of Vitamins in Antibody Production."

August 27: Charles Heidelberger, "Nucleic Acid and Protein Biosynthesis"; David Shemin, "Porphyrin Synthesis"; G. L. Cantoni, "Enzymatic Transmethylations"; S. H. Hutner, "Nutritional Requirements of Various Protozoa."

August 28: M. J. Coon, "Intermediary Metabolism of Amino Acids as Studied with Radio Carbon"; E. C. De Renzo, "The Nature of the Xanthine Oxidase Factor."

CANCER

Alfred Gellhorn, *Chairman*; Albert Tannenbaum, *Vice Chairman*

August 31: J. H. Quastel and A. Cantero, "The Effect of Glucosamine on Tumor Growth"; Harris Busch, "Studies of Oxidative Metabolism of Tumors *in Vivo*"; Jacob Furth, "Character of I^{131} Induced Pituitary Growth; Hormonal and Histological Changes Accompanying Acquisition of Autonomy"; Robert Briggs and Thomas King, "Transplantation of Embryonic Nuclei and the Problem of Nuclear Differentiation."

September 1: Frances L. Haven, "Lipid Metabolism in Tumor-Bearing Animals"; Robert Olson, "Lipogenesis and Lipoprotein in Tumors"; C. Chester Stock, H. C. Reilly, Frederick S. Philips, Sonja Buckley, Donald Clarke, John Ehrlich and Quentin Bartz, "An Anti-Tumor Preparation from a Soil Microorganism. A. Laboratory Investigation"; David A. Karnofsky and James Ewing, "B. Clinical Trials."

September 2: Bjorne Pearson, "Cytochemical Studies During Carcinogenesis"; M. J. Kopac, "Submicro Enzyme Chemistry of Normal and Neoplastic Cells"; Hattie E. Alexander, "A. The Biologic Activity of Desoxyribose Nucleic Acids as Hereditary Determinants in Bacteria"; Stephen Zamenhof, "B. Recent Studies on the Chemistry of Heredity Determination in Bacteria."

September 3: Edwin E. Osgood, "The Physiology of Normal and Leukemic Leukocytes." Other subjects and speakers to be announced.

September 4: Ernest L. Wynder, "Clinical and Experimental Studies on the Etiology of Lung Cancer"; Johannes Clemmesen, "Cancer Endemiology."

Program at New Hampton School

ION EXCHANGE

W. Juda, *Chairman*; J. Schubert, *Vice Chairman*

June 15: Round Table Discussion on New Ion Exchange Materials: *Moderator*: K. W. Pepper; *Participants*: I. M. Abrams, R. E. Anderson, R. Kunin. Symposium on Water Conditioning: M. E. Gilwood, F. K. Lindsay, A. C. Reents.

June 16: Symposium on Water Conditioning: V. J. Calise, T. A. Kirkham, H. P. Gregor, "Non-aqueous Ion Exchange"; W. Cohn, C. Brown, "Biochemical and Medical Applications."

June 17: K. W. Pepper, "Recent European Developments in Ion Exchange Applications"; K. Kraus, "Inorganic Applications"; N. W. Rosenberg, D. Lewis, "Electrochemistry of Ion Exchange Resins."

June 18: G. Scatchard, "Electrochemistry of Ion Exchange Resins"; A. Katchalsky, "Properties of Polyelectrolyte Solutions"; P. Doty, "Properties of Polyelectrolyte Solutions"; W. C. Bauman, "Report on Nomenclature."

June 19: R. A. Ruehrwein, "Synthetic Polyelectrolytes as Soil Conditioning Agents"; A. Opler, "Use of Calculating Machines in the Analysis of Ion Exchange Separations."

NUCLEAR CHEMISTRY

C. D. Coryell, *Chairman*; I. Perlman, *Vice Chairman*

June 22–26: Nuclear Decay Processes: Spectroscopy and Systematics, 3 sessions; Nuclear Fission, 1 session; Transmutation Reactions Including Photonuclear, 2 sessions; Nuclear Techniques: Chemical, 1 session; Nuclear Techniques: Physical, 1 session; Microwave, Atomic Beam, and Spectroscopic Methods, 1 session.

RADIATION CHEMISTRY

Milton Burton, *Chairman*

June 29: Ellison Taylor, *Chairman*; John L. Magee, "Theoretical Introduction, Part I"; Robert L. Platzman, "Theoretical Introduction, Part II"; Milton Burton, "Radiation Chemistry of Organic Mixtures"; Amos S. Newton, "Effects of Structure and Functional Groups in the Radiolysis of Organic Compounds."

June 30: Harold A. Dewhurst, *Chairman*; A. O. Allen, "Review: Radiation Chemistry of Water and Aqueous Inorganic Systems"; J. A. Ghormley and A. C. Stewart, "Radiation Chemistry of Ice"; E. J. Hart, "Radiation Chemistry of Aquo-Organic Solutions"; C. J. Hochanadel, "Radiation Actinometry."

July 1: Wallace Davis, *Chairman*; Fred L. Mahler and Vernon H. Dibeler, "Mass Spectrometer Studies of the Ionization Process"; Benjamin P. Burtt, "Use of Electric Fields in Study of Mechanisms"; W. H. Hamill and R. R. Williams, Jr., "Decomposition of HBr in Presence of Rare Gases"; John E. Willard, "Hot Atom Reactions of Halogens in Hydrocarbon and Alkyl Halide Systems."

July 2: Warren M. Garrison, *Chairman*; Session on techniques. Short uninvited papers exclusively. More detailed program will be given later. This session is to be very informal but the program will be rigidly followed. L. E. Brownell, *Chairman*; Bernard Manowitz, "Nuclear Reactors, Fission Products and Their Possibilities and Limitations for the Industrial Future of Radiation Chemistry"; John G. Trump, "High-Voltage Machines and Their Possibilities and Limitations in the Industrial Future of Radiation Chemistry."

July 3: B. E. Proctor and S. A. Goldblith, "Food and Drug Sterilization"; E. L. Gaden, "Industrial Chemical Potentialities."

INORGANIC CHEMISTRY

E. O. Brimm, *Chairman*; J. J. Katz, *Vice Chairman*

July 6–10: Transition Metal Compounds with Metal-Carbon Bonds: G. Wilkinson, "Organometallic Compounds"; J. Chatt, "Olefin-Addition Compounds"; E. O. Brimm, "Metal Carbonyls."

Mechanisms of Inorganic Reactions: R. E. Connick, "Reactions Involving Electron Transfer"; H. Taube, "Reactions Involving Atom Transfer"; R. G. Pearson, "Substitution Reactions."

Chemical Aspects of Mineral Formation in the Earth's Crust: E. F. Osborn.

Some Aspects of Coordination Chemistry: F. P. Dwyer.

CHEMISTRY AND PHYSICS OF METALS

Harvey Brooks, *Chairman*; J. Goldman, *Vice Chairman*

July 13: Band Theory, Crystal Structure, and Phases: Speaker to be announced, "Alloy Phase Diagrams in Relation to Band Structure"; C. Zener, "Interaction of the Fermi Surface with Brillouin Zone Boundaries and Its Influence on Crystal Structure"; J. C. Slater, "Critique of Band Theory as Applied to Problems of Metallic Structure"; J. O. Betterton and John Frye, "Phase Diagrams and Electronic Structure of Alloys Involving Transition Elements"; H. B. Huntington, "Influence of Electronic Structure on Elastic Constants of Metals"; B.

Averbach, "Electronic Properties of Order-Disorder Systems."

July 14: Modification of Bands by Aperiodic Structures: Speaker to be announced, "Discrete Energy Levels in Metals due to Addition of Foreign Atoms and Its Implications for Band Theory"; D. Pines, "Plasma Oscillations and Electronic Structure of Metals"; J. C. Slater, "Band Structure and Order-Disorder." Magnetic Properties of Conduction Electrons: N. Bloembergen, "Effect of Electronic Paramagnetism on Nuclear Resonance"; C. Kittel, "Free Spin Paramagnetic Resonance in Relation to Electronic Structure."

July 15: Transition Elements: Speaker to be announced, "Energy Bands in Transition Elements"; W. Kohn, "Recent Progress in the Theoretical Calculation of Energy Bands in Transition Elements"; J. Goldman, "Survey of Electronic Specific Heats, Hall Effect, and Magnetic Susceptibility in Transition Elements." Round Table Discussion on Magnetic Structure of Chromium: Fine, Shull, Friedberg, Zener. E. Pugh, "The Hall Effect in Ferromagnetics"; Kriesman, "Magnetic Susceptibility of Transition Elements."

July 16: Optical Properties: L. Apker, "Comparison of Soft-X-Ray Emission and Optical Photoelectric Method for Measuring Density of States"; E. R. Pirori, "Limitations and Advantages of X-Ray Spectroscopy for Determining Electronic Energy Levels in Metals"; Speaker to be announced, "Review of Recent Work on X-Ray Spectroscopy." Electrical Resistivity: Speaker to be announced, "Pressure Effects on the Electrical Resistance of Alloys and Pure Metals"; E. Mendoza, "Thermal and Electrical Conductivity of Non-superconducting Metals at Low Temperatures"; J. Korringa, "Low Temperature Electrical Properties with Special Reference to Solutions of Transition Metals in Noble Metals."

July 17: Ferromagnetism: C. Shull, "Ferromagnetism and Atomic Moments of Transition Metals by Neutron Diffraction"; W. Kleiner, "Theory of Magnetic Form Factor for Neutron Scattering"; R. Weiss, "Atomic Moments in Heusler and Other Alloys."

Microbiological Deterioration

Glenn A. Greathouse, *Chairman*; William J. Robbins and R. E. Vicklund, *Vice Chairmen*

July 20: Studies of Causes of Microbiological Deterioration; Microbiological; Fungi and Bacteria: William J. Robbins, "The More Important Microbiological Agents of Deterioration"; David Gottlieb, "Metabolic Products and Their Relations to Detoxication of the Fungicide or Bactericide." Studies on Prevention of Microbiological Deterioration; Physical-Chemical Aspects of Deterioration Problems: Glenn A. Greathouse, Introductory Remarks; Adrien Albert, "Ionization, pH, and Other Physical Factors in Relation to Biological Activity."

July 21: Chemical Structure and Biological Activity: S. Chaberek, "Theory of Chelation"; Adrien Albert, "Chelation and Its Role in Biological Activity"; S. S. Block, E. G. Kovach, and David Barnes, "Recent Data on Chelating Compounds and Their Biological Activity."

July 22: Harris L. Friedman, "Influence of Isosteric Replacements Upon Biological Activity"; H. O. Halvorson, "Mechanisms of Inhibiting Enzyme Formation by the Use of Amino Acid Analogues." Radioactive Isotopes and Their Role in Preservation Studies: Lawrence P. Miller and S. E. McCallan, "Use of Radioactive Tracers in Determining Rate of Uptake and Dose Required for Inactivating Fungus Spores"; M. M. Baldwin, "Fungicide-Fungi Spore Sorption Studies"; Glenn A. Greathouse and David Barnes, "Radioactive Cellulose and Fungicides and Their Role in Microbiological Deterioration Studies."

July 23: Discussion of Susceptible and Resistant Materials: W. E. Yelland, "Chemical Modification of Cellulose and Its Relation to Biological Activity"; R. H. Bescher, "Wood Preservation"; T. F. Cooke, "Resin Treatment of Cellulosic Fabrics to Prevent Microbiological Deterioration"; J. R. Kanagy, "Leather Preservatives."

July 24: Prediction of Things to Come: Five minutes will be allotted the following to discuss the prediction of things to come in this field of endeavor: William J. Robbins, R. E. Vicklund, Adrien Albert, and other representatives of government, educational, and research institutions, and industry.

Statistics in Chemistry

George E. Kimball, *Chairman*

July 27: Point Estimation and Confidence Intervals.
July 28: Analysis of Variance and Design Experiments.
July 29: Operations Research and Chemistry.
July 30: Statistical Short-Cuts.
July 31: Training Chemists to Use Statistics.

Chemistry of Steroids and Related Natural Products

Carl Djerassi, *Chairman*

August 3: I. E. Bush, "Chromatographic Behavior and Biological Activity of Non-Benzenoid Steroid Hormones as a Function of Structure"; R. N. Jones, "Infrared Spectra and Structure of Steroids"; D. H. R. Barton, "Some Recent Progress in Triterpenoid Chemistry."

August 4: E. R. H. Jones, "Structure of the Polyporenic Acids"; O. Jeger, "Relationship of Tetracyclic Triterpenoids to Steroids"; L. F. Fieser, "Chemistry and Metabolism of Cholesterol and Companions"; R. B. Woodward, Subject to be announced.

August 5: G. Rosenkranz and F. Sondheimer, "Recent Progress in Steroid Chemistry in Mexico"; H. Heusser, "Recent Work in the Field of Steroid Hormones and Related Compounds in Switzerland"; L. H. Sarett, "Total Synthesis of Adrenal Hormones."

August 6: R. B. Turner, "Rearrangements and Stereochemical Properties of Steroids"; J. Fried, "Chemical Studies on Steroidal Microbiological Oxidation Products."

August 7: N. L. Wendler, "Steroid C/D Ring Transformations"; M. Ehrenstein, "Partial Synthesis of Certain Steroid Hormone Analogs."

Analytical Chemistry

Harry Levin, *Chairman*; L. B. Rogers, *Vice Chairman*

Unusual Applications of Analytical Chemistry to the Solution of Problems

August 10: W. E. Campbell, "Communications"; W. Rieman, III, "Analytical Applications of Ion-Exchange Resins."

August 11: H. F. Beeghly, "Ferrous Metals"; Mark G. Inghram, "Chemical and Isotopic Analyses with the Mass Spectrometer as Applied to Geological Problems."

August 12: Norman Wright, "Application of Infrared Analytical Instruments to Plant Production Streams"; W. C. McCrone, Jr., "Microscopy."

August 13: Joseph L. Gormley, "Laboratory Techniques in Criminal Investigations"; Harold A. Frediani, "The Determination of Microgram Quantities of Pharmaceuticals."

August 14: Phillip W. West, "Coordination Chemistry in Analysis and Research."

ORGANIC COATINGS

Henry Grinsfelder, *Chairman*; Lehman Hoag, *Vice Chairman*

August 17: Introductory Remarks: Sam Loshaek, "Basic Considerations Relating to the Kinetics and Extent of Cure in Vinyl Type Coating Materials"; John W. Swanson, "A Study of Film Splitting in Roller Coating Operations"; Harry Burrell, "The Relationship of Theoretical High Polymer Chemistry to the Wrinkle Phenomenon."

August 18: Frank Long, "Diffusion of Water and Solvents in Organic Films"; Edward G. Bobalek, "Electron Microscopy of Pigmented Films."

August 19: D. F. Herman, "Chemistry of the Organotitanium Compounds"; H. H. Beacham, "Utilization of Organotitanium Compounds in Coating Systems"; S. B. Elliot, "Photosensitive Coatings"; John Fletcher, "Practical Considerations of Relationships of Organic Coatings to Vacuum Metalizing of Plastics and Metal Surfaces."

August 20: Ralph J. Wirshing, "Vagaries of Paint Testing"; H. P. Meissner, "Surface Adhesion" (Tentative); Albert G. H. Dietz, "Observations of the Visco Elastic Behavior of High Polymers at Various Rates of Strain and Load Application and Various Temperature Levels" (Tentative).

August 21: G. N. Bruxelles, "Measuring the Gloss of Organic Coatings."

PROTEINS AND NUCLEIC ACIDS

Kurt G. Stern, *Chairman*; M. L. Anson, *Vice Chairman*

August 24: Speaker to be announced, "Relation of Interactions Between Groups Within an Individual Protein or Peptide Molecule and the Configuration of Peptide Chains"; W. T. Astbury, "Interactions Influencing the Folding and Unfolding of Protein Chains, and Relations to Other Protein Interactions"; D. F. Waugh, "Protein-Protein Interactions in Solutions and in Precipitates."

August 25: P. Doty and K. G. Stern, "Reactions of Nucleic Acids and Other Polyelectrolytes with Proteins"; W. H. Stein, "Separation of Proteins by Chromatography"; E. L. Durrum, "Electrophoresis in Immobilized Solvents."

August 26: Speaker to be announced, "Large Scale Fractionation of Proteins"; D. Surgenor, "Fractionation of Proteins by Precipitation with Heavy Metal Salts"; Speaker to be announced, "Role of Combination of Heavy Metal Ions with Proteins in Enzyme Activation and Protein Stabilization."

August 27: I. Klotz, "General Thermodynamic and Structural Theory of Interactions Between Proteins and Ions"; K. Bailey, "Enzymatic Transformations of Proteins into New Proteins"; C. Fromageot, "Controlled Production of Peptides from Proteins."

August 28: Lyman Craig, "Fractionation and Isolation of Peptides"; H. Neurath, "Structure of Peptides as Determined by Enzymatic and Other Methods, Including End Group Methods"; K. Linderstrøm-Lang, "Résumé and Perspectives."

COAL

A. C. Fieldner, *Chairman*; M. A. Elliott, *Vice Chairman*

Coal as a High Polymer

August 31: H. F. Mark, "High Polymer Chemistry Lecture"; A. Gillet, "Coal Polymers"; I. G. C. Dryden, "Solvent Extraction of Coal Polymers."

September 1: Reactions of Coal Polymers: H. H. Storch, "Hydrogenation"; Everett Gorin, "Pyrolysis."

Surface Phenomena in Relation to Coal

September 2: John Turkevich, Lecture, "Concepts and Techniques in Surface Chemistry"; R. B. Anderson, "Sorption and Desorption."

September 3: A. A. Orning, "The Role of Carbon-Oxygen Complexes in the Reactions of Solid Fuels"; Nathaniel Arbiter, "Mineral Flotation Principles"; H. F. Yancey, "Coal Flotation Applications."

Round Table Discussion of Unsolved Problems

September 4: C. R. Kinney, "High Polymer Chemistry of Coal"; N. K. Chaney, "Surface Chemistry of Coal."

Pacific Division Meeting

Robert C. Miller, *Secretary*

Pacific Division

THE 34th annual meeting of the Pacific Division, AAAS, will be held in Santa Barbara, California, June 15–20, 1953. Registration will open Monday morning, June 15, at 9 o'clock, at the Santa Barbara Civic Recreation Center. The Carrillo Hotel has been designated the headquarters hotel. Requests for accommodations at hotels, motels, and auto courts should be sent to the Santa Barbara Convention Bureau.

The presidential address of C. D. Shane, president of the Pacific Division, will be given Tuesday evening, June 16, on "The Distribution of Galaxies in Space." On Wednesday evening, June 17, W. F. Libby of the Institute for Nuclear Studies, University of Chicago, will lecture on "Radiocarbon Dating."

Seventeen societies associated or affiliated with the Pacific Division will participate in the Santa Barbara meeting, with symposia and sessions for submitted papers. There will also be a special symposium Wednesday morning, June 17, on the recent research programs sponsored by the National Research Council through the Pacific Science Board.

Local arrangements are in charge of a General Committee, of which John Cushing, of the University of California at Santa Barbara, is chairman.

The Wiley Bulletin

SCIENCE EDITION

New York — May 8, 1953

TREND TOWARD INTEGRATION IN CONSERVATION EVIDENCED IN FISHERY

More Unity Needed — Ichthyology an Example

Interest in the conservation of our natural resources has steadily increased since Teddy Roosevelt first called attention to the shocking conditions then existing. Wildlife, soils, forests, and fisheries have all been subjects of enlightened legislation. The emphasis to date, however, has been on one or another of these fields, rather than on the over-all conservation picture. There still remains a need to consider conservation as a whole, even though improvement in one field often reflects a similar improvement in another.

This philosophy of unity is reflected in a new book by two authors active in government conservation work: George A. Rounsefell, Department of the Interior, and W. Harry Everhart, University of Maine. In *Fishery Science: Its Methods and Applications,* they treat two fields which, like soil and forest conservation, have developed more or less independently of one another. Marine and freshwater fishery management, say the authors, are essentially the same. No special refinements are necessary in developing and using methods for one or the other. Their new book integrates for the first time the most successful and specialized methods employed in the research, conservation, and management of fishery resources regardless of where the fish occur.

Fishery Science is not meant as a guide to ichthyology. Rather than being an account of the biology of fishes or an application of statistics to biological data, *it presents the problems that confront the administrator, the research worker, the student, and shows how to go about solving them.* It is due for publication this month with approximately 425 pages, and a probable price of $7.50.

ASKED, "WHY WRITE?" AUTHOR EXPLAINS

One often wonders just what causes an author to write a particular book. Not often, however, is one privileged to have the reasons stated as succinctly as does Professor Bradley T. Scheer, University of Oregon, when speaking of his *General Physiology.*

"My decision to write the present book grew out of several years of experience in teaching general physiology, in which I found that none of the available treatments meets the need of a particular group of college and university students."

He speaks of that group which needs a thorough, up-to-date course, shorn of as much irrelevant detail as possible, yet offering a clear exposition of the nature and present status of the basic problems of physiology. His book is written for just such a course.

The author purposely keeps his book concise. He follows facts through to a reasonable conclusion rather than merely listing them. All conclusions reached are based on available evidence, and Professor Scheer makes it a point to distinguish carefully between established facts and tentative conclusions.

General Physiology has 614 pages and is priced at $7.00.

REPORT ON A SUBJECT UNDERLYING ATOMIC RESEARCH

Recent Research in Nuclear Physics Compiled

Much about the recent advances in nuclear physics remains unknown except by those specialists working with it. To help overcome this, Emilio Segrè of the University of California is now editing the second volume of his *Experimental Nuclear Physics,* using the same objectives and in the same manner as in the first volume.

It is patterned after the classic German handbooks, with each section written by an internationally-acknowledged authority on the particular subject under discussion. The purpose is threefold: to present modern experimental techniques; to point out the truly significant facts and data; and to indicate the broad lines of present-day theoretical interpretation.

Volume I has only recently been published (March. 789 pages. $15.00), and Volume II can be expected in August. Slightly smaller in size, it is expected to be about 470 pages, and will probably cost $9.00.

IN STEP WITH RESEARCH

Microwave spectroscopy is among the newest and fastest growing branches in the field of spectroscopy, as almost its entire development has taken place since World War II. Keeping pace with these rapid strides, three professors writing at Duke University: Walter Gordy, William V. Smith, and Ralph Trambarulo, are the first to present the subject in: *Microwave Spectroscopy.*

Summarizing information in various tables, this new book provides the key to an easy familiarity with the instruments and experimental techniques used. It gives a detailed description of significant spectrographic components and supplies the fundamental theory involved in the detection of microwave absorption lines. It provides, moreover, a challenging, valuable key to the results that can be obtained from microwave spectra.

Microwave Spectroscopy will appear this month and have approximately 440 pages. The probable price is $7.50.

"REFRESHING" VIEW OF BASIC SUBJECT

Often basic courses receive little notice merely because they are basic. Like the well-known letter in Poe's tale, they can be in plain sight, but overlooked. It is a welcome occasion, therefore, when a new and "refreshing" text does come along. Such a text, and for just such a course, is *Beginning Algebra for College Students* by Professor Lloyd Lowenstein of Kent State University.

A pre-publication reviewer sums it up when he says, "It reads interestingly and is written in a refreshing way. I enjoyed reading it. The style is good, (the) ideas (are) well expressed in words that give a refreshing and readable quality to the opening of this course in beginning algebra."

Professor Lowenstein makes two points clear. He relates algebra directly to arithmetic. He stresses algebra as a language; a medium of expression. From this approach, the student both learns to use algebra as a tool and to think for himself.

"Lowenstein" is a March publication. It has 279 pages and is priced at $3.50.

Any of the books on this page may be obtained on approval by writing directly to the publishers:
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Meetings & Conferences

May 11–13. Aero Medical Association (Annual). Biltmore Hotel, Los Angeles.
May 11–13. American Association of Petroleum Geologists (Regional). Tulsa, Okla.
May 14. Conference on Instrumentation in Water, Sewage, and Industrial Waste Treatment. Manhattan College, N. Y.
May 14–15. Society for Applied Spectroscopy (Annual). New York.
May 14–23. International Petroleum Exposition. Tulsa.
May 18–22. National Fire Protection Association (Annual). Palmer House, Chicago.
May 18–22. National Tuberculosis Association (Annual). Los Angeles.
May 18–23. International Congress on Electrothermics (3rd). Paris.
May 20–22. National Telemetering Conference. Edgewater Beach Hotel, Chicago.
May 20–22. Society of Photographic Engineers (Annual). U. S. Hotel Thayer, West Point, N. Y.
May 22–23. International Syndical Reunion of Gynecologists and Obstetricians. Paris.
May 24–28. Scientific Apparatus Makers Association (Annual). The Greenbrier, White Sulphur Springs, W. Va.
May 25–28. Air Pollution Control Association (Annual). Lord Baltimore Hotel, Baltimore, Md.
May 25–29. Textile Institute (Annual). Llandudno, Wales.
May 25–30. International Hospital Congress. London.
May 25–30. International Seed Testing Association (10th Congress). Dublin.
May 25–31. World Congress of Fertility and Sterility. Henry Hudson Hotel, New York.
May 28–29. American Rheumatism Association. Waldorf-Astoria, New York.
May 29–31. Field Conference of Pennsylvania Geologists (Annual). Lafayette College, Easton.
May 30–31. Society for Investigative Dermatology (Annual). Hotel Belmont Plaza, New York.
June 1–5. American Medical Association (Annual). New York.
June 4–6. Canadian Society of Microbiologists. Ontario Agricultural College, Guelph.
June 5–6. International Congress of Audiology. Leiden.
June 6–7. International Congress of Bronchology. Utrecht.
June 7–9. American College of Cardiology (Annual). Hotel Statler, Washington, D. C.
June 8–13. International Congress of Otorhinolaryngology (5th). Amsterdam.
June 9–13. American Dermatological Association. Lake Placid Club, Essex County, N. Y.
June 10–12. Research and Development Associates (Annual). Mayflower Hotel, Washington, D. C.
June 10–20. General Chemistry and Analytical Chemistry Workshop. Pennsylvania State College.
June 12–13. Wilson Ornithological Club. Sheboygan, Mich.
June 12–14. American Medical Technologists (Annual). Hotel Hollenden, Cleveland, Ohio.
June 14–18. American Society of Medical Technologists (Annual). Brown Hotel, Louisville, Ky.
June 15–17. American Society of Agricultural Engineers (Annual). William Penn Hotel, Pittsburgh.
June 15–17. American Neurological Association (Annual). Hotel Claridge, Atlantic City, N. J.

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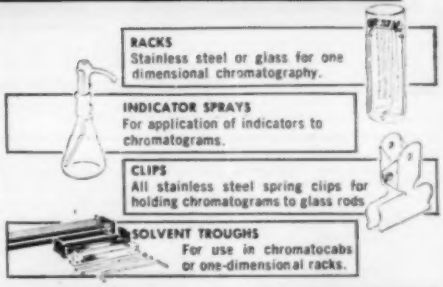

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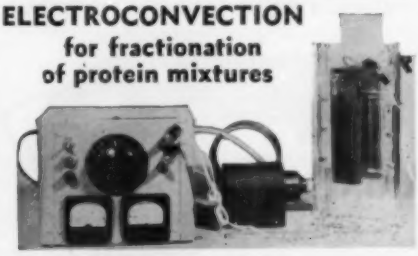

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